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Moderation Analysis of Bowel Function among Nutrients and Physical Function or Depression, as well as whether Bowel Function is Related to Cognition in Older Adults

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by

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ABSTRACT

As we age, the risk for gut issues, such as smooth muscle tone, may be an underlying indirect or direct cause or risk factor for many age-related issues, such as frailty. Consequences of decreased motility and depleted epithelial barrier may result in nutrient deficiencies that may increase the risk for malnutrition (Brownie, 2006). Further, there is increasing evidence that there is a gut-brain-axis relationship that may influence cognition and mental health issues, such as depression and anxiety. While there are relationships established, the interconnections of these factors have yet to be fully understood.

This dissertation examined several relationships specific to nutrient intake, physical function, and depression in older adults while probing for a moderating effect of gut health. Looking further at this theory of the gut-brain bi-directional relationship, an additional gut health assessment was further examined to investigate the relationship with cognitive performance.

Participants were from two separate but complementary data sets. The first data set from the National Health and Nutritional Examination study included a depression outcome analytic sample and a physical function analytic sample who had valid data on nutrient intake, bowel measures, demographic characteristics, depression scores, physical function measurements, and total BMI. The depression analytic sample had a total of 1918 participants with a mean age of 73.76 years, and 1864 participants with a mean age of 73.28 years in the physical function analytic sample. The available nutrients within the data set were further broken down into several different components by a component factor analysis and each component used as a predictor. Two separate bowel measures were examined with one as a fecal incontinence

measure and the other, the Bristol Stool Form Scale, as categorical (normal, constipation, or diarrhea). The second data set, the Nutraceutical Blueberry Study, had a total of 108 participants with a mean age of 73.42 years who had valid data on cognitive measures and a complete gut assessment.

Among the depression analytic sample, there were significant moderating effects of fecal incontinence between several nutrient components and depression after accounting for the control variables. An additional moderated multivariate regression with only the significant components was carried out and resulted in only Component 9 (carbohydrates, sugar, beta-cyrptoxanthin, and vitamin C) and Component 12 (alcohol) having the fecal incontinence measure as a significant moderator with depression as the outcome.

Within the physical function analytical sample, the Bristol Stool Form Scale categorical measure was a significant moderator among Component 6 (MFA22_1, PFA18_4, PFA20_5, PFA22_5, and PFA 22_6) and physical function. Both the constipation and diarrhea categories were related to worse physical function, while in all groups, increase in nutrients from Component 6 resulted in better physical function.

Within the second data set, AVLT and AVLT Delay had a significant quadratic relationship with bowel function. Within the four different groups in the bowel measure (gastric function, gastrointestinal inflammation, small intestine and pancreas, and colon), gastrointestinal inflammation with a negative association and the colon category with a positive association were significant. Among the AVLT Delay, gastrointestinal inflammation was also negatively associated significant predictor.

Outcomes from the current study suggest that fecal incontinence was indicative as a moderator among the first data set, as well as significant predictor for AVLT and AVLT Delayed

in relation to cognition in older adults. Although there were many relationships not found with bowel function as a moderator, the current findings suggest that more thorough measures in additional to microbiota measures could further provide possible directions for new therapeutics in psychological and cognitive therapy, as well as improving physical function in older adults.

CHAPTER ONE:

INTRODUCTION

The function of the gut has been shown to be important for overall health with wide reaching influences. Although it has been shown to have importance, gut function has often been overlooked. The diversity of the microbiota that reside in the gut assist in many bodily processes, such as nutrient absorption and hormone regulation (Yano et al., 2015). Therefore, the gut microbiome helps the body obtain what is essential for the body to maintain overall physical health by absorbing nutrients and minerals. Moreover, prior research has found a bidirectional relationship between gut function and the brain through the vagus nerve and the spinal cord. Therefore, this brain-gut axis has been speculated to have a major role in mental health and cognitive function. Additional research is needed to explore the relationship of the gut function and the mental well-being of individuals. Using functional foods to enhance gut function may be a future option for intervention for both mental health and cognitive health. However, this potential has yet to be realized in human subject research.

In the current dissertation, the relationship between gut/bowel function and physical, mental, and cognitive health will be explored in the two different but complimentary datasets. One of the datasets that will be used is the National Health and Nutrition Examination Survey (NHANES) data from 2005-2010 which is a cross-sectional data set that is thought to nationally represent the United States for the purpose of addressing nutrition, health and disease prevalence. The NHANES data includes Food Frequency Questionnaires to obtain dietary factors, as well as

the Fecal Incontinence Severity Index (FISI) which measures four symptoms that include incontinence of gas, mucus, liquid stool, and solid stool and the Bristol Stool Form Scale that measures stool consistency and be an indicator for gut transit times. Additionally, measures for physical function are assessed by a questionnaire that measures functional limitations that may lead or cause disability that interfere with the ability to work. Mental health is measured using the Patient Health Questionnaire (PHQ-9) which measures the symptoms of depression over the past two weeks. Strengths of this dataset include the large sample size, as well as the dataset being population based. The dataset also includes many biological measures that are useful. As for weaknesses, the dataset has some limitations on the outcome level. The dataset is limited on cognitive measures and is not available in all the years provided.

The second dataset that will be used is the Nutraceutical Blueberry Study data. In this data, gut health is measured by the Health Appraisal Questionnaire Gastrointestinal Health Assessment (HAQ) and cognitive health is measured by several cognitive domains that include episodic memory, processing speed, verbal ability, working memory, executive function, and complex speed. Therefore, the diverse cognitive measures are a great strength of this dataset. A weakness of this data is the measure of gut/bowel function provided and small sample size. The HAQ measure has not been standardized and lacks conciseness of the meaning of the measure. Therefore, precautionary measures of interpretation of the HAQ must be taken into account.

Using these two datasets, the following questions will be addressed:

Research question 1

Using secondary data analysis from the NHANES data set, how mental health (i.e. depression) is related to dietary factors and whether bowel function (fecal incontinence and

bowel consistency) will moderate this relationship will be examined; see Figure 3. It is predicted that those with greater disturbances in their bowel movements and less fiber within their diets will exhibit poorer mental health, such as depression. Additionally, higher carbohydrates and sugar, less vitamin intake, lower unsaturated fats and polyunsaturated fats, and high monounsaturated fats will result in higher rates of depression.

Research question 2

Using secondary data analysis from the NHANES data set, the question on how does certain dietary factors (e.g. carbohydrates) and bowel function (e.g., fecal incontinence or stool type) influence physical health in older adults will be examined; see Figure 4. It is predicted that a diet higher in carbohydrates but low fiber will be related to worse bowel function and physical health based off of previous research. Saturated fats will also be included, and therefore, it is predicted that more unsaturated fats, particularly butanoic, lower monounsaturated fats, and higher polyunsaturated fats will result in better overall physical function and bowel function.

Research question 3

Using data from the Nutraceutical Blueberry Study to assess gut health and the relationship among cognitive health. It is predicted that those with more upsets in their gut health, such as constipation or diarrhea will experience worse cognition versus those who have better gut health.

CHAPTER TWO:

LITERATURE REVIEW

This section will focus on a review of the literature that is pertinent to the questions that will be modeled in the dissertation. First, we will briefly review relevant research on the relationship between age and cognition. Broadly speaking, this will entail the general trends and individual differences among older adults. Second, we will briefly review older adults and physical function maintenance and decline, and how physical function is interrelated to overall function. A brief review of the relevant research pertaining to older adults and mental health, such as depression, will be discussed. Also included will be a brief review of gut/bowel function in relation to cognition and diet in age related research.

Cognition and aging

The older adult population will increase by approximately 50% in the upcoming years (Vincent & Velkoff, 2010) and with increased age, there is an increased risk for neurodegenerative diseases and chronic diseases (Hebert, Scherr, Bienias, Bennett, & Evans, 2003). This will dramatically increase the need for healthcare services in the future. In addition to researching risk factors for neurodegenerative diseases, it is also important to understand normal age-related cognitive changes in older adults to distinguish the difference between the two. Understanding normal age-related cognitive changes will further the knowledge of what is

abnormal and what risk factors we can identify to start therapeutic interventions (Harada, Natelson Love, & Triebel, 2013).

Normal age-related cognitive changes can be very discouraging for older adults since one may worry about further deterioration of his/her cognitive abilities. These cognitive changes have been shown to vary in the change and rate of decline. This has been shown in speed of processing and perceptual reasoning in which there are declines as a normal part of aging, but the rate of decline and age in which decline begins is not the same for all (Hultsch, MacDonald, & Dixon, 2002; Mackinnon, Christensen, Hofer, Korten, & Jorm, 2003; Wisdom, Mignogna, & Collins, 2012). Processing speed has been shown to be inter-related with other cognitive domains (Finkel, Reynolds, McArdle, & Pedersen, 2007; Salthouse, 1996). Therefore, processing speed may play a large role in why there is cognitive decline in older adults. Processing speed is also considered a part of fluid intelligence which has been shown to decrease with aging.

There have been several studies that have recognized the differences in the cognitive performance of older adults that are more physical active than those who are not. For example, Benedict and colleagues (2013) have found a difference in brain structures using an MRI and increased verbal fluency in those who are more physically active. Additionally, research has found greater brain volume and reduced risk of Alzheimer's disease in those who are more active (Colcombe et al., 2003; Geda, Roberts, Knopman, & et al., 2010).

In relation to aging and cognitive decline, the cognitive reserve hypothesis suggests that there are lifestyle factors that may impact how long cognition is preserved before there is any age related decline (Marioni et al., 2014; Singh-Manoux et al., 2011). The preservation of cognitive abilities and the rate of decline has come from research studies entailing those with Alzheimer's disease (Scarmeas & Stern, 2004; Tucker & Stern, 2011). Those with higher cognitive reserve

have shown to have a decreased risk for age-related cognitive decline while those with low cognitive reserve may not have the compensatory neural network to stave off brain pathology (Lopez et al., 2014). In addition to preserving cognitive function in aging individuals, cognitive reserve has also been shown to protect cognitive function in individuals that have immune deficiency and are obese (Galioto, Alosco, Spitznagel, Stanek, & Gunstad, 2013). Cognitive reserve has even been explored as being a buffer against mental illness, such as depression (Coloma & Zihl, 2014). Education has been shown to be a protective factor for a better cognitive reserve, but there may be other significant negative and positive factors not yet recognized.

Attention and whether age impacts this cognitive ability also depends on what the task/tasks are at hand. Complex tasks that may need more divided attention may show a decline in older adults. Multiple tasks may take more cognitive resources and therefore, be harder to effectively complete the tasks at hand causing decreased attention (Rogers & Monsell, 1995). Many of these decreased cognitive abilities seen in older adults may also be a large reason why there are age differences seen in memory, as well. The different types of memory also have different trajectories throughout the life span. For example, semantic memory may remain stable until very old age (Rönnlund, Nyberg, Bäckman, & Nilsson, 2005). Executive function is also very important for older adults everyday functioning. Executive function is largely involved in planning and reasoning. Many tasks that do include executive function entail a speed component. Therefore, evidence of an age difference in executive function in those who are older adults is not surprising (Libon et al., 1994).

As a result of the impairments in cognitive performance that older adults face, recent attention has examined interventions to slow the decline. Several interventions have been evaluated including cognitive training, lifestyle enrichment, and dietary interventions. For

example, cognitive improvements have been found with the Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) data. A recent study conducted by Rebok and colleagues (2014) conducted a follow-up of the individuals who have participated in the ACTIVE study who went through cognitive training and booster training to improve cognitive function. The results have shown improvements in instrumental activities of daily living, reasoning, and speed of processing (Rebok et al., 2014). Other programs that focus on keeping older adults physically and mentally productive is the John Hopkins University Baltimore Experience Corps. The Baltimore Experience Corps takes a further approach as a possible intervention technique by enriching the older adults' environment with intergenerational interaction. The program initiates the productivity of older adults to use their knowledge and skills to help future generations. This keeps older adults' brains active while giving a sense of purpose by helping others ("Baltimore Experience Corps® Study," 2014). Other interventions for older adults to enhance cognitive performance have included nutraceutical supplements, such as NT-020. A study conducted by Small and colleagues (2014) indicated a significant association with processing speed with the use of the supplement, NT-020, when compared with a placebo control (Small et al., 2014). In addition to dietary and cognitive training, exercise programs have also been examined as potential interventions for older adults and preventing cognitive decline. Exercise programs have ranged from yoga to aerobic fitness that have shown improvement in cognitive function in older adults (Gothe, Kramer, & McAuley, 2014; Voss et al., 2013). As for specific dietary patterns, one of the most abundant diets that have been extensively researched involves the Mediterranean Diet (MED). Those who had greater adherence to the MED over time have also seen benefits in cognitive health and decreased risk in Alzheimer's disease. A total of 1,393 cognitively healthy were included in the study and followed over the duration of

approximately 4.5 years. After controlling for age, education, caloric intake, body mass intake, cohort, gender, and ethnic group there was a significant association with adherence to the MED and mild cognitive impairment (MCI). Additionally, it was also found that those who were determined to develop MCI over the course of the study were less likely to develop Alzheimer's disease (Scarmeas et al., 2009). These benefits have also been established in many other longitudinal studies, as well (Gao et al., 2007; Tangney et al., 2011). The MED seems like a viable alternative to medications and an excellent preventative tool for cognitive decline in older adults. How to increase adherence could greatly enhance the older adult population in the United States.

Physical health and older adults

As a normal part of aging, there are declines in physical health within older adults. Although these declines in physical health would like to be avoided, some are just an inevitable part of the aging process. Research has shown that decreased physical health is related to more chronic diseases, as well as frailty (K. Rockwood, Song, & Mitnitski, 2011). In relation to memory, physical function of an older adult has also been shown to be protective to certain cognitive demands (Tian et al., 2014). Physical health has also been shown to be a significant predictor for the survival of older adults (Mossakowska et al., 2014). This extends the importance of sustaining physical health as long as possible. It is important to identify what the most common problems are with physical health and whether or not these declines may be avoided or decline at a slower rate. Therefore, seeking certain lifestyle changes and interventions to strengthen one's physical health is important. Further, older adults remaining independent as

long as possible could help deter health care costs in the future while maintaining older adults' mental well-being.

The process of aging is thought to have an accumulating effect on the physical function of an individual. Identifying which factors that contribute to physical function of individuals would help create interventions and narrow areas to focus on. Although knowing risk factors, following a holistic approach to aging could target all areas including mental well-being. Research has shown that those who are considered frailer are more likely to have a higher mortality rate. In turn, those who are considered more physically fit have a slower rate of decline and lower rates of mortality. Again, looking at mortality among the physical fit versus those who are frail adds to the idea that these factors may be accumulative at different rates depending on an individual's physical function (K. Rockwood et al., 2011).

When describing factors that may influence physical health, these can include many areas among the lifestyle that may be manipulated. Therefore, these lifestyle influences would be useful targets for interventions. Nutrition has been found to influence physical health in older adults. In addition to diet, there are more internal factors that are influenced by the diet, such as insulin levels or gut function (McNulty et al., 2013; Nettleton et al., 2013). As discussed previously with aging and cognition, the MED has been found to be associated with decreased cancer risk, CVD, and beneficial to reduce neurodegenerative disease (Castañer et al., 2013; Psaltopoulou et al., 2004; Sofi, Macchi, Abbate, Gensini, & Casini, 2010; Trichopoulou, Lagiou, Kuper, & Trichopoulos, 2000). There have been repeated studies to show the potential implications of the MED that could benefit those with CVD. With the increase in chronic diseases and obesity rates, the MED has been investigated in the United States population. A rather large longitudinal study was conducted by the National Institutes of Health (NIH) – AARP

Diet and Health Study over the time span of 10 years. Those who adhered to a diet that resembled food patterns associated with the MED had a decreased cardiovascular mortality compared to those who did not have an associated pattern with the MED. Even further, benefits were seen with an inverse association of cancer and all-cause mortality (Mitrou, Kipnis, Thiébaut, & et al., 2007). Adherence to the MED seems to be the key in the majority of studies. The Nurses Health Study also examined if the MED is protective to CVD. Those participants who resembled the MED and maintained it the longest had the most significant advantage based on examination of quintiles (Fung et al., 2009). In addition to preventing CVD, adherence to the MED has shown to reduce the delirious consequences in those who already have CVD. Therefore, the MED may be an optimal intervention for those with or at risk for cardiovascular problems (Barzi et al., 2003).

Frailty, aside from disability, has shown to be related to cognitive function in older adults, as well. The relationship is not clear on whether frailty leads to cognitive decline or if cognitive decline leads to frailty, but the influence of both factors have been found to lead to future problems, such as disability and additional age-related issues (Atkinson et al., 2005). Atkinson and colleagues (2005) examined women over a three year period that showed that frailty was a risk factor that increased the risk of cognitive related issues and physical decline. Therefore, prevention and reliable measures for frailty and cognition are rather important for the projected physical function of an older adult.

Mental well-being and older adults

An older adult's mental well-being is a very important key to living a meaningful life even in the midst of disability. With an increase in chronic diseases among the American

population, the risk of mental issues may become more prevalent (Salive, 2013). By targeting mental well-being in older adults, rehabilitative methods and different health conditions one may endure may result in better outcomes (Nordbakke & Schwanen, 2013). Physical health, dietary choices, and social interaction may all be very useful in preserving a healthy mental well-being or improving what mental well-being one may have (Blanchflower, Oswald, & Stewart-Brown, 2013; Pilkington, Windsor, & Crisp, 2012; Ziegler & Schwanen, 2011). The next few paragraphs will address different aspects of older adults' mental well-being, such as, quality of life.

There are many risk factors associated with the mental well-being of older adults. Factors that are innate include age and gender while others are more lifestyle oriented. Older age in itself may not initially result in depression, but there has been indication that in those 80 years and older may have an increased risk for depression (Byles, Gallienne, Blyth, & Banks, 2012). Atkins and colleagues (2013) examined psychological distress and quality of life in older adults from an Australian sample. A reoccurring theme for mental well-being and quality of life in older adults tends to be physical function status. Additionally, sleep quality has been found as an indicator of mental well-being and cognitive function (Moore, Adler, Williams, & Jackson, 2002; Nebes, Buysse, Halligan, Houck, & Monk, 2009). Social support has also been found to buffer poor mental well-being in prior research (Atkins et al., 2013; Newsom & Schulz, 1996).

The risk of depression may greatly increase with aging, as well as increase the risk of decreased physical function (Penninx et al., 1998). On the other hand, depression in itself may impact an individual's functionality and lead to other progressive illnesses over the course of his/her lifetime (Alexopoulos et al., 2002; Bruce, Seeman, Merrill, & Blazer, 1994). This interrelationship among disability and depression has shown to be an important issue to address given the discourse of the interaction of the two (Bruce et al., 1994; Von Korff, Ormel, Katon, &

Lin, 1992). Depression may also increase the risk of dementia, which is a growing issue within our aging population (Diniz, Butters, Albert, Dew, & Reynolds, 2013; Prince et al., 2013). With already rising healthcare costs in the older adult population, mental health, especially depression, can add to the burden of the healthcare costs in one's lifetime (Katon, Lin, Russo, & Unutzer, 2003).

Nutrition and older adults

An additional risk factor that may deserve further attention is dietary factors that influence the health of older adults. It is well known that an individual's diet is a major determinant in the development in the aging process (Joseph et al., 1998). Physiologically, older adults may not retain nutrients as well as they use to, therefore, close monitoring of one's diet is needed (Barberger-Gateau et al., 2007). Further, malnourishment may occur in older adults, especially those with Alzheimer's disease (Navratilova et al., 2013). Recognizing what types of dietary factors may work as potential dietary interventions may be applicable to prevent or slow the progression of cognitive decline associated with both normal age-related cognitive change and neurodegenerative diseases. To prevent exacerbated healthcare costs in the future, further development of preventative strategies and interventions deserve more attention (Suehs et al., 2013). Depletion of certain nutrients may lead to other problems later on in life. Older adults may be at a higher risk for nutritional deficiencies due to metabolic function and gut mobility. Additionally, with the increase risk of chronic disease in the United States and across the world, may lead to more complications to nutrition (Lochner & Cox, 2013; Patel et al., 2013).

An individual's diet has been associated with being overweight and obese, as well as metabolic syndrome (Buckman et al., 2014; Leibowitz, Rehman, Paradis, & Schiffrin, 2013).

Metabolic syndrome is closely related to several disorders, such as diabetes type 2, due to the syndrome resulting in insulin resistance, pro-inflammatory state, dyslipidemia, and high blood pressure (Eckel, Grundy, & Zimmet, 2005; Tonkin, 2004). A recent review investigated factors related to overweight and obesity and whether those individuals could still be "healthy". It was reported that even in the absence of metabolic factors, those being overweight and obese individuals were still at risk for high all-cause mortality (Kramer, Zinman, & Retnakaran, 2013). Additionally, Kramer and colleagues found that having an unhealthy metabolic status increased the risk for all-cause mortality and cardiovascular events regardless of having normal weight or being overweight. Further, obesity and metabolic syndrome has been associated with cognitive deficits (Simopoulos, 2013). For example, Gatto and colleagues (2008) examined older adults who were diagnosed with metabolic syndrome and cognitive function. These individuals were free of diabetes or cardiovascular disease (CVD). Findings resulted in an association between metabolic syndrome and worse cognitive performance compared to those who did not have metabolic syndrome. Specifically, verbal learning, semantic memory, and global cognition decreased among those with metabolic syndrome. Metabolic syndrome and obesity both relate to decreased cognition and all-cause mortality both independently and in relation to each other. Therefore, these findings support the need and importance of future dietary interventions, even for those who have poor diets, but normal weight.

Gut health and bowel function in older adults

An area of interest that has received lot of attention recently has been the relationship of gut microbiota and an individual's overall health throughout the life course. For example, at childbirth, the type of birthing process and where the birth occurred can impact that infant long

after just the first few years of life, such as developing allergies (Dominguez-Bello et al., 2010; Roduit et al., 2009; van Nimwegen et al., 2011). On the opposite end of the spectrum, it has been found that gut microbiota may be protective in chronic diseases and impact physical health in late age (Claesson et al., 2012). When examining specific issues with older adults that relate to bowel health, many considerations need to be taken into account, such as gastric motility, consistency, and how this impacts nutrient absorption and metabolites, as well as the relationship among the residing gut microbiota. The gut does contain a protective barrier provided by epithelial cells and mucus. This barrier is important in providing a defense against things such as, inflammation and unwanted xenobiotics that may preside in the environment (Tocchetti, Rigalli, Arana, Villanueva, & Mottino, 2016). As with older adults, research has shown that age is related to a depleted mucosal barrier in gastric systems (Mabbott et al., 2015; E. L. Mitchell et al., 2016). Possible issues, such as diabetes or inflammation may be due to this compromised gut barrier and functionality (Vaarala, Atkinson, & Neu, 2008).

Gut-brain axis

Not only has gut microbiota been related to overall health, but more specifically, gut microbiota has been investigated in relation to cognition and brain health (Cryan & Dinan, 2012). Additionally, there have been studies released that have reported an association with mental status and disorders, such as anxiety, associated with gut microbiota (Heijtz et al., 2011; Neufeld, Kang, Bienenstock, & Foster, 2011). Even more groundbreaking is the current finding that gut microbiota has been related to autism (Gilbert, Krajmalnik-Brown, Porazinska, Weiss, & Knight, 2013). Although just in the past few years has this idea of the gut-brain axis really taken off at an exponential speed in research interests, there has been speculation of this relationship.

Much of the findings found within this area of research is strengthening the idea that this is an area that is multi-disciplinary in a sense of the bio-psycho-social model (Wilhelmsen, 2000). You can think of the gut-brain axis as a theory in itself in relation to what was not previously widely accepted prior to many of these investigations. Investigation of the role of the vagus nerve has demonstrated that there is a relationship between the gut and brain in prior research. The 10th cranial nerve, the vagus nerve, innervates the colon and has a major role in gut functions that relays information up the brainstem. The vagus nerve has additionally been demonstrated to be a factor in learning and memories (K. B. Clark, Naritoku, Smith, Browning, & Jensen, 1999). Based on an evolutionary approach, the polyvagal theory is based on the vagus nerve having many influences on the bodily processes that range from heart function to stress response reactivity and how this relates to visceral homeostasis as a central regulatory component. Although, this theory is more based in explaining the social engagement system that help regulate social interaction reactivity with facial muscles, the theory could be a bridge to other influences, such as mental health and gut function (Porges, 2009). The dorsal vagal complex is largely associated with these digestive processes and the vagal nerve processes. In the dorsal vagal complex, oxytocin and vasopressin function are involved in the vagal nerve cross-talk among the digestive tract and brain. Therefore, this is a possible direct or indirect route for modulating motility and a target for stress and other hormonal balances (Porges, 2001). Even further, research has focused on the relationship with dietary factors, gut microbiota, and brain health (Aziz, Dore, Emmanuel, Guarner, & Quigley, 2013; Das, 2010). Investigating the gut-brain axis may give insight into future interventions for treating or preventing cognitive decline in OAs. Even further, manipulation of the gut microbiota or replenishing the gut microbiota may have significant implications for future treatments involving neurodegenerative disorders.

Composition of gut microbiota

Metagenomic sequencing, which is an alternative to rRNA sequencing, has recognized a few million gut microbial genes (Qin et al., 2010). There are three main clusters of gut microbiota, *Bacteroidetes*, *Firmicutes* and *Actinobacteria* that vary in numbers in everyone. *Bacteroides* are speculated to be very important since they consist of 30% of the gut microbiome (Salyers, 1984). Each individual also has his/her own unique gut microbiome that is influenced by his/her own unique lifestyle (Arumugam et al., 2011; Eckburg et al., 2005). Previous findings have found that changes over the life course, there is a shift to more *Bacteroidetes* and fewer *Firmicutes* (Hsiao et al., 2013). *Bacteroides* are gram-negative anaerobic bacterium and can produce polysaccharides which are complex carbohydrates, such as cellulose (Wexler, 2007). Additionally, *Bifidobacterium, eubacterium, clostridium, peptococcus, and peptostreptococcus* have also been found within humans (Salminen et al., 1998; Simon & Gorbach, 1984). There are many more microbiota species that are not as abundant, but may be key sources to examine future treatments. Many of these species, such as *Faecalibacterium prausnitzii*, have shown to have anti-inflammatory properties (Sokol et al., 2008). Categorization of these different enterotypes, or clusters, might have been oversimplified in the past. The overall picture may be more complicated than what Arumugam and colleagues (2011) found, and it is suggested that there is much more diversity and complexity to the human microbiome (Jeffery, Claesson, O'Toole, & Shanahan, 2012). Current researchers among this field acknowledge that there is still substantial amount of gut microbiota to be identified.

In addition to what is unknown in regards to the composition, the evolutionary theory takes a step back and directly addresses diversity of the gut microbiota as a whole. The idea of the theory is that diversity in the gut maintains a healthy balance to the point where one specific

microbiota species does not have too much influence. If a species was to take over the status quo, the species would manipulate biological processes in favor of maintaining or increasing its numbers (Wasielewski, Alcock, & Aktipis, 2016).

Alternative measures may be less costly than the methods mentioned above. There are stool measures that include consistency ratings and bowel patterns. The Bristol Stool Scale, which has been found to measure transit time of the colon, was examined to determine whether such a measure could be representative of gut microbiota composition (Vandeputte et al., 2016). The results of this comparison study on the relationship with these enterotypes (bacterial classification), species richness or diversity, and distribution among the different categories of the Bristol Stool Form supported the hypothesis that this bowel measure had matching associations among the certain types and richness of gut bacteria. Therefore, such a measure could be deemed an alternative representation of the gut microbiota composition on a broad scale (Vandeputte et al., 2015). Furthermore, a more recent study examined stool frequency instead of consistency in comparison to gut microbiota measurements and found similar results (Hadizadeh et al., 2016). In a similar study that examined similar factors as the previous study described, similar findings were found with the bacterial composition but the Bristol Stool Scale lacked an association with the bacterial richness as found in Vandeputte and colleagues research (Tigchelaar et al., 2015)

Gut microbiota and immune system

The relationship with gut microbiota and the immune system has been investigated in relation to the physiological processes within our bodies. It has been established the immune system is very important for an individual's health and can impact disorders such as,

neurological, irritable bowel syndrome (IBS), obesity, type 2 diabetes, and metabolic syndrome (Chassaing & Gewirtz, 2013; Galimberti, Schoonenboom, Scheltens, & et al., 2006; Gasque, Dean, McGreal, VanBeek, & Morgan, 2000; Kau, Ahern, Griffin, Goodman, & Gordon, 2011; Musso, Gambino, & Cassader, 2011). Many factors such as antibiotic use and diet have been shown to impact the relationship between the immune system, gut microbiota diversity, and health (Chassaing & Gewirtz, 2013). Also, in the aging population there is a concern for a weakened immune system and, therefore, the investigation of gut microbiota and the immune system may bring light to this important connection to health (Salvioli et al., 2013). Further, how gut microbiota may impact cognition through an immune response should be considered, as well.

OAs have more digestive issues than their younger counterparts (Delvaux, 2003). Digestive systems need proper management to counteract some of the age-associated problems. Inflammatory properties associated with the gut microbiota and epithelial barrier have been recognized. With the change in gut microbiota in OAs, there may be an increase in the inflammatory response that is not as common in younger adults (Magrone & Jirillo, 2013).

In regulated intestinal microbiota, there is a homeostasis that retains a symbiosis of the gut that does not cause a constant inflammatory response. Further, the epithelial layer in not impaired and there is a balance among commensal bacteria, such as *Bacteroides* (Eckburg et al., 2005). Within the gut associated lymphoid tissue, which is the digestive tract's first line of defense, contains the intestinal epithelial cells. When an invasive counterpart is recognized, there is a release of mucosal host defenses such as, defensins, which is activated by toll-like receptors (TLRs) (Miron & Cristea, 2012). TLRs have a role in the maintenance of the immune system with the help of pattern-recognition receptors. When there is an introduction of a pathogen, this can induce inflammation (Akira & Takeda, 2004). TLRs are also important for the innate and

adaptive immune system. Gut microbiota have shown to have an impact on influencing the Th1/Th2 cell balance. This has been found with *Bacteroides fragilis*. The normal composition of the gut microbiome contains *Bacteroides fragilis* and are usually abundant. *Bacteroide fragilis* produces polysaccharide A (PSA), which has an impact on these TLRs that impact the Th1/Th2 balance. PSA is further influenced by antigen presenting cells that have shown to have a protective role by correcting an imbalance of Th1/Th2 in disease states (Ochoa-Repáraz et al., 2010; Q. Wang et al., 2006).

Therefore, homeostasis of commensal bacteria could play a powerful role in protective immunity or may result in a high inflammatory response, such as inflammatory bowel disease (Hanauer, 2006). Commensal bacteria play an essential role in the Th1/Th2 cell balance. With OAs, this immune response is weakened, and the entry of pathogens may cause an increase in pro-inflammatory cytokines. This, therefore, produces a low-grade inflammation that may be damaging overtime (Biagi et al., 2013; Larbi et al., 2008). In conclusion, further investigation of the influence of the gut and the immune system could help further a clearer understanding of the role on overall health.

Gut microbiota, diet, and obesity

Change in one's gut microbiota has shown to impact one's metabolic activity. Therefore, this can greatly impact one's energy supply (Li et al., 2008). Gut microbiota utilize carbohydrates that are not digested initially and are transferred to short chain fatty acids (SCFAs). The SCFAs play a major role in maintaining homeostasis within the gut. Butyrate, a SCFA, is one of the main sources for energy supply for intestinal epithelial cells (McNeil, 1984). OAs have been found to have decreased butyrate and therefore, may impact overall health.

Research has found that decreased butyrate has been associated with increased inflammation and a precursor to colon health problems due to an increase in harmful metabolites, such as ammonia (Hippe et al., 2011). Lactate may also be utilized by gut microbiota to form butyrate, but when there is not a gut homeostasis maintained, sulfate reducing bacteria may utilize the lactate along with hydrogen to form hydrogen sulfide (Marquet, Duncan, Chassard, Bernalier-Donadille, & Flint, 2009). Hydrogen sulfide has been found to be harmful to commensal bacteria and possibly leading to DNA damage (Attene-Ramos, Wagner, Plewa, & Gaskins, 2006). Lactate accumulation has also been found to be abundant among OAs. The amount of fiber one incorporates in his/her diet can have significant implications on this energy supply of butyrate. High fiber diets have been shown to be beneficial for overall gut health and help with gut microbiota diversity. Conversely, OAs have been found to lack a fiber rich diet (Laurin, Brodeur, Bourdages, Vallée, & Lachapelle, 1994). Therefore, OAs may need additional fiber intake and dietary guidance to maintain healthy digestion.

There has been a connection made with the type of diet one has and the composition of one's gut microbiota. A study that administered dietary questionnaires and measured gut microbiota composition found that diets higher in fiber resulted in more *Firmicutes* and *Proteobacteria* while lower in fiber and protein consumption was associated with higher composition of *Bacteroidetes* and *Actinobacteria*. Higher *Prevotella* was associated with diets that resembled more of a carbohydrate-based diet. Interestingly, a recent study just identified *Prevotella copri* to be highly abundant in those with autoimmune diseases, especially rheumatoid arthritis (Scher et al., 2013). There was also rapid change in the gut microbiota when measuring the composition within 24 hours, while measuring the gut microbiota composition after 10 days did not change the enterotype composition. Diet clearly influenced gut microbiota and timing has

been demonstrated to vary. The study demonstrates that there may be rapid change induced by dietary changes, but other studies have also found that long-term diet can change enterotype clustering (Wu et al., 2011). Examining the shift in gut microbiota and the timing will be important considerations to take when developing interventions in the future to improve one's health.

Gut microbiota & physical function

Physical function is largely a concern in the aging population and avoiding decline over time. Several issues can plague older adults that result in possible disability and loss of autonomy. The role of muscle mass can largely impact the trajectory of such physical declines. The gut microbiota has been a possible target to mediate the depletion of muscle in individuals due to influence on muscle cells. Several metabolites and pathways produced by gut microbiota have been demonstrated to play an indirect role in muscle mass. For example, bile acids are a metabolite that influences energy expenditure and toll-like receptors (TLR) involved in muscle mass that involve maintenance or depletion (Bindels & Delzenne, 2013). More recently in an animal model, there is evidence of a metabolite, urolithan A, that was found to largely influence mitochondrial and muscle function indicating the importance of the gut microbiota and metabolite connection in aging (Ryu et al., 2016). Gut microbiota has also been speculated to be a determinant in malnutrition, which is often seen in older adults and cancer and muscle wasting (Million, Diallo, & Raoult, 2016). Ultimately, gut microbiota is showing that many of the mechanisms involved are largely interconnected in overall physiological processes.

Fecal incontinence and older adults

Fecal incontinence can be a debilitating condition that interferes with everyday activities, as well as be an indicator of a further underlying problem (O'Keefe, Talley, Zinsmeister, & Jacobsen, 1995). Fecal incontinence can also become an issue where there is no underlying etiology that can be specified while some are related to nerve damage or antibiotic use (Chassagne et al., 1999; Rao, 2004). With the aging population, the risk for developing issues with fecal incontinence increases which could interfere with quality of life and possible malnourishment (Bartlett, Nowak, & Ho, 2009; Nelson, Norton, Cautley, & Furner, 1995; Saka, Kaya, Ozturk, Erten, & Karan, 2010). Bowel disorders, such as irritable bowel syndrome (IBS), is an example of issues related to incontinence may have a more underlying psychological aspect to the symptoms (Longstreth & Wolde-Tsadik, 1993). Although, there has been more recent findings that the current state of the gut microbiota is highly related to IBS (Kassinen et al., 2007; Shukla, Ghoshal, Dhole, & Ghoshal, 2015). In relation to bowel disorders, several studies are identifying the role microbiota have in the issues associated with the bowel and finding an established dysbiosis of the gut (Marchesi et al., 2016). The dysbiotic bowel syndrome has been a newly coined term that may help target new therapeutics involving fecal incontinence entity type disorders (Benno et al., 2016). Targeting dysbiosis, which is related to digestion and the off balance of gut microbiota, may have broad reaching effects including fecal incontinence. Gut microbiota has been finding more interconnections with the whole body processes, including nerve function and how functional foods, such as prebiotics, may establish a more regular bowel movement process as well as increased sense of regulated sensitivity (Ranson & Saffrey, 2015).

These are broad implications, but may be of great use for interventions if found to be a target for incontinence issues.

Gut microbiota and interventions

Research clearly shows that gut microbiota has an impact overall health on a broad spectrum. Extensive research still needs to be conducted to establish the safety of treatments involving administration of gut microbiota. A clear establishment of the enterotypes and influence of specific gut microbiota still needs to be investigated. Future interventions may benefit from including measures of gut microbiota along with other factors being investigated. Additionally, functional foods that contain natural probiotics, such as kombucha, may assist OAs in assisted living facilities and nursing homes to maintain a healthy gut microbiota and strong immune systems. Researching the potential mind altering abilities that gut microbiota may have on cognitive performance may also warrant new directions in the research field. Gut microbiota may also hold new ground in problems associated with antibiotic use. Perhaps gut microbiota has been the missing link to assist interventions from infants to OAs, and this is just the beginning to new and innovative treatments.

There may be specific foods that act as natural prebiotics and probiotics that can be taken into combination to replenish the gut microbiome without interfering with the already established gut microbiota there. Since older adults have a shift in healthy gut microbiota and decreased diversity, probiotics may be ideal especially for older adults (Pérez Martínez, Bäuerl, & Collado, 2014). Finding which microbial strains are the most effective is still needed. Among studies, there has been evidence of inter-individual variation among response to prebiotics. Therefore, investigating why some benefit from prebiotics and others do not is needed. Further, using probiotics along with prebiotics may have significant impact on health in a beneficial way rather

than using probiotics or prebiotics alone. Research clearly shows that gut microbiota has an influence on many factors that impact overall health from obesity to CNS diseases. Extensive research still needs to be conducted to establish the safety of treatments involving administration of gut microbiota. A clear establishment of the enterotypes and influence of specific gut microbiota still needs to be investigated. Perhaps gut microbiota has been the missing link to assist interventions from infants to older adults and this is just the beginning to new and innovative treatments.

Summary

As aging results, there is a plethora of age-related issues that may occur. Aging may be inevitable, but how people experience that process may be intervened resulting in a longer health span. Chronic disease and cognitive decline are becoming increasingly a concern with a growing older adult population. By exploring a wider approach to physiological changes in the aging process, new capable approaches may become available. Determining what lifestyle factors may influence cognition and other chronic disease, such as dietary factors, and by showing stronger evidence of these factors, will help push such lifestyle influences in the medical field. As more evidence unveils the gut and brain inter-relationship and what may modify this relationship, there will be further clarification of where the next new innovation in interventions should go. By using the NHANES data and the Nutraceutical Blueberry Study data, questions will be addressed about the associations among dietary factors, physical function, mental well-being, cognition, and gut/bowel function specifically in older adults. Within the NHANES depression analytic sample, predictions will be aligned with prior research to suggest that a healthier diet will result in lower depression scores, as well as bowel function will indicate as a significant moderator

among these relationships. Secondly, healthier diet will be predicted to be associated with better physical functioning with bowel function as a significant moderator in the NHANES physical function analytical sample. Among the relationship among cognition and bowel function, it will be predicted that worse bowel scores will indicate to be related to worse cognitive performance among older adults with the Nutraceutical Blueberry Study data set.

Therefore, to reiterate, questions being addressed will be with two separate data sets, the NHANES data set (2005-2010) and the Nutraceutical Blueberry Study data set. More specifically, examining dietary factors (e.g. sugar consumption) and bowel function in relation to depression in older adults will be examined in the NHANES. The second question addressed within the same data set will include examination of physical function in relation to bowel function and diet. The third question addressed will include the second data set, the Nutraceutical Blueberry Study, which will examine self-reported gut/bowel function and the relationship among cognitive health. These two data sets are complementary to the three questions that will be addressed due to limitations among one or the other set. Therefore, each data set seemingly picks up gaps where the other data set lacks.

CHAPTER THREE:

METHOD

National Health and Nutrition Examination Survey

The NHANES is a continuous survey conducted by the U.S. National Center for Health Statistics of the Centers for Disease Control and Prevention since 1999 (National Center for Health & United States Public Health, 1963). Although continuous, a new wave of participants are included every two years (e.g. 2005-2006, 2007-2008). A four-stage sampling design is carried out, in which counties are first picked at random, then an area randomly within that county, followed by random households chosen within the segments, and finally, the actual individuals in the chosen household. The laboratory subsamples are selected at random according to each protocol component of interest based on a fraction of the total examined group (Johnson et al., 2013).

Categories of race and ethnicity included Mexican American, non-Hispanic black, non-Hispanic white, other Hispanic, and other race including multi-racial. These race and ethnicity categories were recoded to indicate those who were non-Hispanic white and all other race and ethinicity as non-white for the analysis. Education was categorized as less than 9th grade, 9-11 grade education (includes 12th grade no diploma), high school graduate/GED, some college or associates degree, and college graduate or higher. Education was recoded to an ordinal variable

to indicate the level of education for each individual. A brief description of study variables, and laboratory methods are included here, but are described in detail elsewhere (Johnson et al., 2013).

Measures

Dietary recall

Dietary data collection is collected through 24-hour dietary recall interview over two days. The first day is administered in addition with other measures during the Mobile Examination Center exam. The dietary portion is administered through dietary interviewers. The second day 24-hour dietary recall interview is collected by telephone after 3-10 days of the initial dietary recall. The 24-hour dietary recall included information specific to what types of food and beverages were consumed specifically on that day and how, for example, where and when the food was eaten and how much was consumed. During the beginning of the interview, participants are given an open response to what their diet was like for that day. After this response, the interviewer pushes for any types of food that might have been forgotten which specifically addressed 9 categories which were nonalcoholic beverages, alcoholic beverages, sweets, savory snacks, fruit and vegetables and cheeses, breads and rolls, and any other foods. Next, the time and occasion of the participant's diet would be detailed and a final probe for anything that should be additionally included.

The Food Frequency Questionnaire (FFQ) was self-report after the participants received the questionnaire in the mail. The FFQ focuses on the participants' dietary consumption during the previous 12 months. Specific foods, such as whole grain foods, was also included. Data was processed by the USDA's Food and Nutrient Database for Dietary Studies where total nutrient

intakes were computed. Data coders were highly qualified and measures were taken to ensure quality of the data (Bodner-Montville, Ahuja, Ingwersen, & Haggerty, 2006; Anand, Raper, & Tong, 2006). The list of fatty acids included within the study categorized by saturated, polyunsaturated, and monounsaturated can be found in Figure 1.

Mental health

The depression screen questionnaire (DPQ) was given to those who were 12 years or older. The specific questionnaire, Patient Health Questionnaire (PHQ-9), has been validated as an appropriate measure for detecting depression. The questionnaire asks participants to refer to their previous two weeks and answer a total of ten questions including one on functional limitations. The answer choices ranged from 0-3 with 0 being not at all, 1 being several days, 2 as more than half the days, and 3 being nearly everyday. With a possible score of 27, a score of 10 or higher is considered clinical depression.

Bowel health questionnaire

The bowel health questionnaire (BHQ) includes those participants who are 20 years and older. There was an additional Bristol Stool Form Scale component.

Fecal incontinence measure

The BHQ addresses questions related to the number of bowel movements associated with gas, mucus, liquid stool, and solid stool and fecal incontinence. The participants were given an answer choice from two or more times a day, once a day, two or more times a week, once a week, one to three times a month, and never. The fifth question is directly related to how often

one has any type of bowel movement in a day which was not included in the overall calculation of total bowel health. The answers were reverse coded to indicate higher values as worse bowel health. A Fecal Incontinence Severity Index (FISI) score is used to identify severity of incontinence (T. H. Rockwood et al., 1999).

Bristol Stool Form Scale

The Bristol Stool Form Scale is a rating scale of bowel consistency that is most common in an individual and has been fully validated (Lewis & Heaton, 1997). There are seven types of stool consistencies to choose from according to the chart; see Figure 2. The measure is to identify stool consistency, as well as be an indicator for gut transit time (Heaton & O'Donnell, 1994). Further, three categories were formed from the seven types of stool. Type 1 and Type 2 were categorized as the constipation group, Type 3, Type 4, and Type 5 were indicated as the normal category, and Type 6 and Type 7 were categorized as diarrhea group.

Physical functioning

The physical functioning questionnaire (PFQ) was administered to those 20 years or older in age. The purpose of the PFQ is to identify any level of disability through physical, mental, and/or illness. A physical activity is provided, and the participant chooses from no difficulty, some difficulty, much difficulty, unable to do, or do not do this activity. In addition to identifying physical limitations, what condition may be the reason for the limitations are also asked. For example, a participant may list up to three, such as, diabetes, arthritis, and heart disease. How frequent these conditions cause limitations are asked towards the end of the questionnaire. Higher scores indicated worse physical functioning.

Statistical Analyses

Statistical analysis were performed using IBM SPSS Statistics 21 analytical software. Data were cleaned and checked for missing data along with any outliers. Tests for normality, linearity, and homoscedasticity were established. The sample for the analysis will only contain those 65 and older. Descriptive statistics will be performed among the sample and reported. Correlational matrices will be examined for preliminary relationships. In both the depression analytical sample and physical function analtyical sample, control variables included age, race, gender, education, physical activity, calories, BMI, supplement use, antacid use, on a special diet, and prescription drug use. For the physical function analytical sample, depression was also included as a control variable. For the nutrient independent variables that were available in the NHANES data set from 2005-2010, a factor analysis was utilized to further compact the variables into specific components and decrease the number of independent variables overall. Components were formed based on the inter-correlations that were given within the factor analysis output. All independent variables were matched on a component with a .4 or higher correlation.

Research Question 1 – Part A:

Does bowel function and nutrients interact as moderators to depression?

Statistical analyses are to be examined among dietary factors (see Table 2) and mental health (depression) in older adults with an additional variable, bowel function, to indicate any moderation among the relationship. Any categorical variables were recoded to be meaningful within the analysis. In relation to each individual nutrient included within the study, log-

transformation was performed to decrease the skewness and kurtosis. Due to the abundance of nutrients provided in the data, a factorial analysis was conducted to create grouping components.

Moderation was tested using the analytic tool created by Andrew Hayes (Hayes, 2013). This tool is an additive function for different data software, such as SPSS. To examine if the interaction among dietary factors and bowel function were indicative of depression in older adults, a moderated regression using PROCESS including the control variables was conducted. The PROCESS add-on mean centers the data that, therefore, allowing the conditional effect of the independent variable and moderator to be interpreted when the other variable is at the sample mean (Hayes, 2013). To identify significance of an interaction and at what levels, the Johnson-Neyman technique was generated along with the analysis.

Research Question 1 – Part B:

Does Bristol Stool Form Scale categories; normal, constipation, and diarrhea/loose stools moderate the relationship among nutrients and depression?

Statistical analyses are to be examined among dietary factors (see Table 2) and mental health (depression) in older adults with an additional variable, Bristol Stool Form Scale, to indicate any moderation among the relationship. Any categorical variables were recoded to be meaningful within the analysis. In relation to each individual nutrient included within the study, log-transformation was performed to decrease the skewness and kurtosis. Due to the abundance of nutrients provided in the data, a factorial analysis was conducted to create grouping components. The Bristol Stool Scale was categorized into three different groups. Those with Type 1 and Type 2 were categorized to a constipation group, those with Type 3, Type 4, and

Type 5 were considered to be in the normal bowel group, and Type 6 and Type 7 were categorized as diarrhea/loose stools group.

Moderation was tested using the analytic tool created by Andrew Hayes (Hayes, 2013). This tool is an additive function for different data software, such as SPSS. To examine if the interaction among dietary factors and the Bristol Stool categories were indicative of depression in older adults, a moderated regression using PROCESS including the control variables was conducted. To identify significance of an interaction and at what levels, the R-square change due to interaction was examined and the conditional effect of each Bristol Stool category examined.

Research Question 2 – Part A:

Does bowel function and nutrients interact as moderators to physical function?

Statistical analyses are to be examined among dietary factors (see Table 17) and physical function in older adults with an additional variable, bowel function, to indicate any moderation among the relationship. Any categorical variables were recoded to be meaningful within the analysis. In relation to each individual nutrient included within the study, log-transformation was performed to decrease the skewness and kurtosis. Due to the abundance of nutrients provided in the data, a factorial analysis was conducted to create grouping components. An interaction term was created among the dietary component variables and bowel function. To examine if the interaction among dietary factors and bowel function were indicative of physical function in older adults, a moderated multiple regression was conducted adjusting for covariates (age, ethnicity, gender, education, BMI, physical activity, and calaories).

Moderation was tested using the analytic tool created by Andrew Hayes (Hayes, 2013). This tool is an additive function for different data software, such as SPSS. To examine if the

interaction among dietary factors and bowel function were indicative of physical function in older adults, a moderated regression using PROCESS including the control variables was conducted. To identify significance of an interaction and at what levels, the Johnson-Neyman technique was generated along with the analysis.

Research Question 2 – Part B:

Does Bristol Stool Form Scale categories; normal, constipation, and diarrhea/loose stools moderate the relationship among nutrients and physical function?

Statistical analyses are to be examined among dietary factors (see Table 2) and physical function in older adults with an additional variable, Bristol Stool Form Scale, to indicate any moderation among the relationship. Any categorical variables were recoded to be meaningful within the analysis. In relation to each individual nutrient included within the study, log-transformation was performed to decrease the skewness and kurtosis. Due to the abundance of nutrients provided in the data, a factorial analysis was conducted to create grouping components. The Bristol Stool Scale was categorized into three different groups. Those with Type 1 and Type 2 were categorized to a constipation group, those with Type 3, Type 4, and Type 5 were considered to be in the normal bowel group, and Type 6 and Type 7 were categorized as diarrhea/loose stools group.

Moderation was tested using the analytic tool created by Andrew Hayes (Hayes, 2013). This tool is an additive function for different data software, such as SPSS. To examine if the interaction among dietary factors and the Bristol Stool categories were indicative of depression in older adults, a moderated regression using PROCESS including the control variables was

conducted. To identify significance of an interaction and at what levels, the R-square change due to interaction was examined and the conditional effect of each Bristol Stool category examined.

Nutraceutical blueberry study approach

Participant recruitment for the Nutraceutical Blueberry Study clinical trial involved utilizing several outreach methods, such as memory screening events and local newspaper advertisements. Inclusion criteria for the study were ages 65–85 years, native English speaking, able to comprehend and sign the informed consent, and lack of dementia that was determined using the Mini-Mental State Examination. Participants were excluded from the study if there were any known allergies to the ingredients of the study supplements, antioxidant supplements other than what is provided in the trial would not be stopped, or any indication of depression indicated by the Center for Epidemiologic Studies–Depression scale.

Screening

Description information collected during the screening process included basic demographic information, allergies, and any medical history a particpant may have. As used in many studies, the MMSE was used as a screening tool that provide an indication of global cognitive performance among participants in which participants had to receive a score of 24 or better to continue on in the study. Self-reported health status was evaluated using the SF-12 Health survey. Finally, depressive symptoms were assessed using the 10-item Centers for Epidemiologic Studies Depression Scale (CES-D).

Cognition

Six different tests were administered to obtain cognitive data in episodic memory, processing speed, verbal ability, working memory, executive function, and complex speed. The Auditory Verbal Learning Test (AVLT) was used to measure episodic memory in the sample. The first part of the AVLT included reading a list of 15 common English words and remembering these words for the purpose of recall. This first task was used to measure immediate recall (average number of words recalled across five learning trials). The second part of the task was for the participant to attempt to recall those same words after a 20 minute delay. Verbal ability was established by giving a word and indication to choose a synonym for that given word from a total of five options. Processing speed was measured using the Identical Pictures Test, the Number Comparision task, and Trail Making A. For Trail Making A, an inverse transformation was applied to scores before standardization to account for this measure recording latency, rather than number correct. Working memory provides an index of the ability to maintain some information in memory while simultaneously manipulating other information and was measured with the Forward and Backward Digit Span task. Executive functioning includes skills that are involved in the planning and execution of cognitive tasks and was measured with Trail Making B, Category Fluency, and Controlled Oral Word Association. For Trail Making B, an inverse transformation was applied in the same manner as Trail Making A. Finally, we assessed complex speed, which assesses the ability to do multiple mental tasks quickly using the number of correct items from the Digit Symbol Test.

Gut health

The Gastrointestinal (GI) Health Assement Health Appraisal Questionnaire (HAQ) Part I (GIHAQ) is a questionnaire originally developed as a marketing and clinical tool for the healthcare setting. The GIHAQ is an extension created in 2006 from the original HAQ developed in 1983 by Lyra Heller, Michael Katke, and Tim Katke (Cartagine, 2011). The GIHAQ requires particpants to indicate how their gut health has been in the past four months. The questionnaire consists of four different sections representing gastric function (Section A, 7 questions), gastrointestinal inflammation (Section B, 9 questions), small intestine and pancreas (Section C, 10 questions), and the colon (Section D, 9 questions). These questions for each category have been decided among these three health professionals based on their expertise and as a tool to represent the concept of functional medicine. Additionally, the gastrointestinal health questionnaire is used for marketing and clinic use. This questionnaire is intended to be an initial assessment of patients experiencing health issues and is used in conjunction with other health assessments. Participants were required to indicate from four answer choices assigned points that included no/rarely (0 points), occasionally (1 point), often (4 points), or frequently (8 points). Within each section, the total points added up are to be an indication of the extent of priority that should be given pertaining to each area of gut health that is considered. Among gastric function (Section A), 1-3 points are low priority, 4-7 points moderate priority, and 8-56 points are considered high priority. Gastrointestinal Inflammation (Section B) had a range of points from 0-72 with 1-3 points considered low priority, 4-7 points moderate priority, and 8 points or more is high priority. Section C, small intestine and pancreas, possible points ranged from 0-80. Low priority was considered 0-7 points, high priority was 8-15 points, and high priority was 16 points and higher. The last section involving the colon (section D) had an overall range from 0-72

points. Low priority consideration included 0-7 points, moderate priority 8-15 points, and high priority was 16 points and higher. The questionnaire has never been validated, therefore interpretation must be taken with caution.

Statistical Analyses

Statistical analysis will be performed using IBM SPSS Statistics 21 analytical software. Data will be cleaned and checked for missing data. Tests for normality, linearity, and homoscedasticity will be established. Descriptive statistics will be performed among the sample and reported.

Research Question 3:

Is there a relationship among gut health and cognitive performance?

To examine if gut health were indicative of cognition (episodic memory, processing speed, verbal ability, working memory, executive functioning, and complex speed), a stepwise regression was conducted adjusting for covariates (age, gender, ethnicity, and education) in Model 1. Model 2 included the predictor gut health to identify influence on cognition. Quadratic effects of the bowel measure was further examined in Model 3. These steps are to be completed with each cognitive domain as the dependent variable.

Statistical power and sample size

Using G*Power 3.1., power analyses were examined for sufficient effect size in multiple regression analyses in the Nutraceutical Blueberry Study. The sample size recommendation was

up to eight predictors and sample size recommendation of 52 individuals to achieve 80% power, two-tailed *p*-value = .05, and large effect size (0.35) (Cohen, 1992).

CHAPTER FOUR:

RESULTS

Within this section, results will be displayed for the sample demographic characteristics for each separate question. Next, results will be described for each research question thereafter, as well as with the corresponding tables and figures.

Question 1 A and B sample characteristics - Depression

The first question examined the relationship between depression and the dietary components by using the NHANES data set. The sample size for this question (n = 1918) included those participants who were 65 and older, had dietary data and bowel data, and all demographic variables. Figure 5 includes how many were missing due to lack of criteria and the breakdown of the sample. The sample was mostly white (66.5%), although a well diverse sample, more females (56.3%), the majority high school graduates or more education, an average of 73.76 years of age, a mean score of 3.85 on the depression screener questionnaire and only 10% considered clinically depressed, and a mean score of 3.04 on the fecal incontinence measure; see Table 1. The dietary characteistics and fatty acid amounts of the sample can be found in Table 2 and Table 3 respectively. Within Table 4, the bowel characteristics of the sample show that most participants fell under the normal condition subtype. The average number of bowel movements in the depression analytic sample was approxiametly 9 (M = 9.08, SD = 5.45) in one week.

Correlations were conducted among the variables in question for control variables and the outcome variable, depression. Among the demographic variables, being younger, being White, being male, and having more education was significantly related to less depression. Being more physically active, not being on a special diet, and more calories were also related to less depression. Specific correlational values can be found on Table 5. Correlations between the control variables and the continuous bowel measure can also be found in Table 5. Being white, being on a special diet, and more calories was related to higher scores on the continuous bowel measure. Additional correlations among the control variables and dietary varaibles are listed in Table 6 and fatty acids corelations in Table 7. The list for significant correlations among the dietary variables and depression can be found in Table 8. The majority of the dietary variables had a significant negative assocation with depression except for calcium while a few, such as, sugars, cholesterol, lycopene, caffeine, theobromine, meat, and coffee, were not. Correlations among the fatty acids and depression are listed in Table 9. In addition to the correlations, a one-way analysis of variance among Bristol Stool From Scale, which is broken into three categories, and depression was conducted. Among Bristol Stool and depression, there were significant differences among the groups. The normal category was significantly different from the diarrhea/loose stools category and the constipation group reached near significance ($p = .081$) compared to the normal category. There were no significant differences among constipation and the diarrhea/loose stool categories in relation to depression.

Next, component variables were formed using the dietary predictors in question. A total of thirteen components were formed from the original 53 dietary predictors. The factor anlaysis rotation matrix for the depression analytic sample can be found in Table 10. Each independent variable had a factor loading of .4 or higher. Component 1 consists of all the short chain fatty

acids (SFA). Component 2 consists of fiber, calcium, phosphorus, magnesium, zinc, copper, and potassium. Thiamin, riboflavin, niacin, vitmain B6, folate, folic acid, vitamin B12, and iron form component 3. Total fat, vitamin E, sodium, monounsaturated fatty acid (MFA) 18_1, MFA20_1, Polyunsaturated fatty acid (PFA) 18_2, and PFA18_3 consist of component 4. Component 5 includes protein, cholesterol, choline, selenium, MFA16_1, and PFA20_4. The sixth component includes alpha carotene, beta carotene, lutein, and vitamin K. Component 7 contains MFA22_1, PFA18_4, PFA20_5, PFA22_5, and PFA22_6. Retinol and vitamin A are within Component 8. Component 9 includes carbohydrates, sugar, beta-crypto-xanthin, and vitamin C. Component 10 only consists of lycopenen, as well as Component 11 with theobromine, Component 12 with alcohol, and Component 13 with caffeine. This list can be found in Table 11.

Question 1 part A - Control variables

The control variables used within the regression moderation analysis included age, race, gender, education, physical activity, calories, BMI, supplement use, antacid use, on a special diet, and prescription drug use. Only race, education, physical activity, and calories were significant predictors of depression. Age was near significant at the $p = .073$ level and special diet at the $p = .058$ level. These results indicated that being younger, non-white, being less educated, being less active, consuming less calories, and being on a special diet resulted in higher levels of depression; see Table 5.

Question 1 part A – Moderated regression

Results for the moderated regression with each component as a predictor variable for the outcome depression and fecal incontinence as a moderator resulted in Component 2 (fiber,

calcium, phosphorus, magnesium, zinc, copper, and potassium), Component 3 (thiamin, riboflavin, niacin, vitamin B6, folate, folic acid, vitamin B12, and iron), Component 4 (total fat, vitamin E, sodium, MFA18_1, MFA20_1, PFA18_2, and PFA18_3), Component 5 (protein, cholesterol, choline, selenium, MFA16_1, and PFA 20_4), Component 6 (alpha carotene, beta carotene, lutein, and vitamin K), Component 9 (carbohydrates, sugar, beta-crypto-xanthin, and vitamin C), and Component 12 (alcohol) as statistically significant for fecal incontinence as a moderator; see Table 12. The significant moderated regressions will be further discussed below.

Component 2 – Fiber, Calcium, Phosphorus, Magnesium, Zinc, Copper, and Potassium. The overall model was significant ($F(14, 1927) = 7.919$, $p < .001$, $R_2 = .060$) with fecal incontinence (B = 0.213, $SE_B = 0.044$, $p < .001$) as significant. The interaction (B = -0.484, $SE_B = 0.273$, $p = .077$) reached near significance. The R-square increase due to interaction reached near significance adding .3% variance to the overall model ($F(1, 1927) = 3.129$, $p = .077$, $\Delta R^2 = 0.003$). This indicates that with increased issues with fecal incontinence, there is a greater effect on the relationship among Component 2 and depression; see Table 13. The Johnson-Neyman significance regions indicated that values at 3.271 and above on the bowel measure was indicative of having a moderating effect between the relationship Component 2 and Depression.

Component 3 – Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Folic Acid, Vitamin B12, and Iron. The overall model was significant ($F(14, 1927) = 8.089$, $p < .001$, $R_2 = .063$) and fecal incontinence (B = 0.209, $SE_B = 0.043$, $p < .001$), Component 3 (B = -1.704, $SE_B = .0628$, $p = .007$) and the interaction (B = -0.513, $SE_B = 0.247$, $p = .038$) were significant predictors of depression. The R-square increase due to interaction was significant ($F(1, 1927) = 4.311$, $p = .038$, $\Delta R^2 = 0.003$). Therefore, an increase in bowel issues increased the relationship among Component 3 and depression resulting in an increase in depression; see Table 13. The Johnson-

Neyman significance regions indicate values at 2.125 and above sifnificantly moderates the relationship among Component 3 and depression.

Component 4 – Total Fat, Vitamin E, Sodium, MFA18_1, MFA20_1, PFA18_2, and PFA18_3. The overall model was significant ($F(14, 1927) = 7.888$, $p < .001$, $R_2 = .063$) accounting for 6.3% of the variance. Fecal incontinence (B = 0.219, $SE_B = 0.044$, $p < .001$), Component 4 (B = -2.036, $SE_B = 1.021$, $p = .046$), the interaction term (B = -0.578, $SE_B = 0.259$, $p = .026$), and R-square increase due to the interaction ($F(1, 1927) = 4.973$, $p = .026$, $\Delta R^2 = 0.004$) were significant. Therefore, fecal incontinence significantly moderated the relationship among Component 4 and depression with higher numbers of the bowel measure being associated with having a larger moderating effect; see Table 13. The moderating effect of the bowel measure becomes significant at the value of 2.657 and above as demonstrated in the Johnson-Neyman technique.

Component 5 – Protein, Cholesterol, Choline, Selenium, MFA16_1, and PFA20_4. There was a significant overall model ($F(14, 1927) = 7.953$, $p < .001$, $R_2 = 0.061$) indicating that the predictors explained 6.1% of the variance for the outcome variable, depression. Fecal incontinence (B = 0.213, $SE_B = 0.044$, $p < .001$), Component 5 (B = -1.317, $SE_B = 0.659$, $p = 0.046$), the interaction term (B = -0.505, $SE_B = 0.252$, $p = .046$), and R-square increase due to the interaction ($F(1, 1927) = 4.005$, $p = .046$, $\Delta R^2 = 0.003$) were significant. As represented in Table 13, the increase in bowel issues had a greater moderating effect on the relationship among Component 5 and depression. The Johnson-Neyman technique indicated values 3.188 and above had a significant conditional effect of Component 5 on Depression.

Component 6 – Alpha Carotene, Beta Carotene, Lutein, and Vitamin K. There was a significant overall model ($F(14, 1927) = 8.065$, $p < .001$, $R_2 = 0.064$) indicating that the

predictors explained 6.4% of the variance for the outcome variable, depression. Fecal incontinence (B = 0.219, SE_B = 0.044, p < .001), Component 6 (B = -0.483, SE_B = 0.182, p = .008), the interaction term (B = -0.183, SE_B = 0.091, p = .045), and R-square increase due to the interaction (F(1, 1927) = 4.030, p = .045, ΔR^2 = 0.004) were significant. As represented in Table 13, the increase in bowel issues had a greater moderating effect on the relationship among Component 6 and depression. Moderator values defining Johnson-Neyman significance regions are values 2.255 and above.

Component 9 – Carbohydrates, Sugar, Beta-Cryptoxanthin, and Vitamin C. The overall model was significant (F(14, 1927) = 7.968, p < .001, R_2 = .064) accounting for 6.4% of the variance. Fecal incontinence (B = 0.209, SE_B = 0.042, p < .001), the interaction term (B = -0.365, SE_B = 0.141, p = .011), and R-square increase due to the interaction (F(1, 1927) = 6.691, p = .011, ΔR^2 = 0.006) were significant. Component 9 reached near significant (B = -0.557, SE_B = 0.295, p = 0.059). Therefore, fecal incontinence significantly moderated the relationship among Component 9 and depression. Higher numbers of fecal incontinence were associated with higher depression among the association with Component 9; see Table 13. The Johnson-Neyman technique indicates values 3.056 and higher on the bowel measure had a significant conditional effect on Component 9 on Depression. Figure 6 demonstrates the differences in depression depending on low or high fecal incontinence as a moderator and Component 9.

Component 12 - Alcohol. The overall model was significant (F(14, 1927) = 8.174, p < .001, R_2 = .060) accounting for 6% of the variance. Fecal incontinence (B = 0.214, SE_B = 0.043, p < .001), Component 12 (B = -0.316, SE_B = 0.151, p = 0.037), the interaction term (B = -0.142 SE_B = 0.064, p = .027), and R-square increase due to the interaction (F(1, 1927) = 4.916, p = .027, ΔR^2 = 0.002) were significant. Therefore, fecal incontinence significantly moderated the

relationship among Component 12 and depression. Higher numbers of fecal incontinence were associated with higher depression among the association with Component 12; see Table 13. The Johnson-Neyman technique indicated bowel measure values of 3.212 and higher significantly moderate the conditional effect of Component 12 on depression. Figure 7 demonstrates the differences in depression depending on low or high fecal incontinence as a moderator and Component 12.

Vegetable Consumption - The overall model was significant ($F(14, 1927) = 8.341$, $p < .001$, $R_2 = .063$) accounting for 6.3% of the variance. Fecal incontinence (B = 0.216, SE_B = 0.044, $p < .001$), total vegetable intake (B = -0.001, SE_B = 0.001, $p = .008$), the interaction term (B = -0.000, SE_B = 0.000, $p = .041$), and R-square increase due to the interaction ($F(1, 1927) = 4.231$, $p = .041$, $\Delta R^2 = 0.002$) were significant. Therefore, fecal incontinence significantly moderated the relationship among vegetable intake amount and depression. Higher numbers of fecal incontinence were associated with higher depression among the association with vegetable amounts; see Table 13. The Johnson-Neyman technique indicates values 1.783 and higher on the bowel measure had a significant conditional effect on vegetable intake amounts on Depression. Figure 8 demonstrates the differences in depression depending on low or high fecal incontinence as a moderator and vegetable intake.

Question 1 part B – Moderated regression

Results for the moderated regression analysis with each component as the predictor variable for the outcome, depression, only indicated a near significant moderating effect of Bristol Stool with Component 6 (Alpha carotene, beta carotene, lutein, and vitamin K) and Component 11 (Theobromine). The results for all components can be found in Table 14. Among

component 6, only group 1, constipation category, was shown to have a significant conditional effect and group 2, normal category, was near significant, $p = .088$. The conditional effect of Bristol Stool categories on Component 6 and physical function can be found in Figure 9. Within the conditional effect of Bristol Stool among Component 11 and physical function, only constipation and the normal bowel group were near significant. The contitional effect of Bristol Stool categories on Component 11 and physical function can be found in Figure 10.

Question 1 summary

Among the fecal incontinence measure, it was shown to be a significant moderator for Component 3, Component 4, Component 5, Component 6, Component 9, Component 12, and vegetable intake with depression as the outcome variable. Component 2 reached near significance with fecal incontinence as a moderator. The additional multivariate moderated regression analysis identified Component 9 (carbohydrates, sugars, beta-cryptoxanthin, and vitamin K) and Component 12 (alcohol) as the most significant predictors when all significant components were placed in the model all at the same time.

The Bristol Stool Form measure with three different categories as moderators; constipation, normal, and the diarrhea group, were shown to be near significant among Component 6 (alpha carotene, beta carotene, lutein, and vitamin K) and Component 11 (theobromine). All other nutrient components and individual food groups were non-significant.

Question 2 A and B sample characteristics - Physical function

Among the second question addressed using the NHANES data set and physical function as the outcome variable, the final total of participants ($N = 1763$) used included those participants

who were 65 and older, had dietary data and bowel data, and all demographic variables. Figure 5 includes how many were missing due to lack of criteria and the breakdown of the sample. The sample consisted of approximately half female, the majority high school graduates or more education, 64.9% white, an average age of 73.28 years, a mean score of 21.33 on physical function (higher scores are worse with a possible score of 0-80), and an average score of 1.59 on the fecal incontinence questionnaire (possible score of 1-20). The descriptives can be found in Table 15. Descriptives for the bowel characteristics of the sample may be found in Table 16 and the dietary characteristics in Table 17. The average number of bowel movements in the physical function analytic sample was approxiametly 9 (M = 9.20, SD = 4.85) in one week. Fatty acid characteristics for the physical function analytical sample can be found in Table 18.

Correlations were conducted among the variables in question for control variables and the outcome variable, physical function. Among the demographic variables, being older, female, and less educated was associated with poorer physical function. Being less physically active, a higher BMI, more depressed, and less calories were associated with worse physical function scores, and therefore, be included in the analysis as control variables. Specific correlational values can be found on Table 19. Having higher education, more calories, supplement use, being on a special diet, and being depressed was associated with worse fecal incontinence scores. Correlations between the control variables and the continuous bowel measure can be found in Table 19. Additional correlations among the control variables and dietary measures are listed in Table 20 and fatty acid corelations in Table 21. The list for significant correlations among the dietary variables and physical function can be found in Table 22. With most dietary variables significantly related to physical function, less of a particular nutrient was related to worse physical function scores, except for carbohydrates and copper in which more was related to

worse physical function. Only retinol, alpha carotene, folic acid, caffeine, and theobromine were not significantly correlated with physcial function. Correlations among the fatty acids and physical function are listed in Table 23. In addition to the correlations, a one-way analysis of variance among Bristol Stool From Scale, which is broken into three categories, and physical function was conducted. Among Bristol Stool and Physical Function, there were significant differences among the groups of normal bowel and constipation, as well as near significant differences among the diarrhea group and normal group.

Next, composite variables were formed using the dietary predictors in question. A total of twelve components were formed from the original 53 dietary predictors. All predictors were included within a component based on a factor loading of .4 or higher. The factor anlaysis rotation matrix for the physical function analytic sample can be found in Table 24. Component 1 consists of thiamin, riboflavin, niacin, vitamin B6, folate, folic acid, vitamin B12, calcium, phosphorus, potassium, iron, sodium, and zinc. Component 2 consists of all short-chain fatty acids. Protein, cholesterol, choline, selenium, MFA16_1, and PFA20_1 form component 3. Total fat, vitamin E, MFA18_1, MFA20_1, PFA18_1, PFA18_3 consist of component 4. Component 5 includes alpha carotene, beta carotene, beta-cryptoxanthin, lutein, vitamin C, and vitamin K. The sixth component includes MFA22_1, PFA18_4, PFA20_5, PFA22_5, and PFA22_6. Component 7 contains fiber, magnesium, and copper. Carbohydrates, sugar, and theobromine are within Component 8. Component 9 includes vitamin A and retinol. Component 10 only consists of lycopene, as well as Component 11 with alcohol, and Component 12 with caffeine. This list can be found in Table 25.

Question 2 part A - Control variables

The control variables used within the regression moderation analysis included age, ethnicity, gender, education, physical activity, calories, BMI, supplement use, antacid use, being on a special diet, prescription drug use, and depression. Only age, gender, education, BMI, physical activity, prescription drug use, and depression were significant predictors of physical function. These results indicated that being older, female, being less educated, having a higher BMI, being less active, no prescription drug use, and higher depression scores resulted in worse physical function; see Table 19.

Question 2 part A – Moderated regression

Moderated regression were ran separately for each different component and physical funciton as the outcome. Among the moderated regression ran with the continuous fecal incontinence scores being questioned as a moderator among the predictor and outcome, there were no significant moderating effects indicated. The results of these outcomes can be found in Table 26.

Question 2 part B – Moderated regression

Results for the moderated regression analysis with each component as the predictor variable for the outcome, physical function, only indicated a significant moderating effect of Bristol Stool with Component 6 (MFA22_1, PFA18_4, PFA20_5, PFA22_5, and PFA22_6) and near significant moderating effect with Component 9 (vitamin A and retinol). The results for all components can be found in Table 27. The conditional effect of Bristol Stool categories on

Component 9 and physical function can be found in Figure 12. Only the constipation group was shown to be near significant (p = .060).

Component 6 – MFA22_1, PFA18_4, PFA20_5, PFA22_5, and PFA22_6. The overall model was significant (F(17, 1745) = 11.192, p < .001, R_2 = .125) with Component 6 (B = -13.103, SE_B = 6.241, p =.036) as sigificant. Among the categorical variable, Bristol Stool, there was a near significant R-square increase due to interaction (F(2, 1745) = 4.975, p = .007, ΔR_2 = 0.003). The conditional effect of the focal predictor in groups defined by the moderator variable can be found in Figure 11. The constipation group and diarrhea/loose stools were significant as a conditional effect on the relationship among Component 6 and physical function.

Question 2 summary

Among the two separate moderator variables, continous fecal incontinence measure and the Bristol Stool categories, only Bristol Stool was a significant moderator among Component 6 (MFA22_1, PFA18_4, PFA20_5, PFA22_5, and PFA22_6) and physical function. Constipation was the only significant group out of the three categories, constipation, normal, and diarrhea. Higher scores of component 6 and those in the constipation group were related to higher depression scores.

Research question 3 – Sample characteristics

Question 3 included the control variables of gender, ethnicity, age, and education for each separate regression. Each separate regression included an individual cognitive measure as the outcome and the predictor variable, the bowel function questionnaire, contained four different sections used each as a predictor variable. These four sections included gastric function,

gastrointestinal inflammation, small intestines and pancreas, and colon. The overall sample consisted of mostly white, an average of approximately 15 years of education, 66% female, and an average age of 73.42 years; see Table 28. Among the four categories within the bowel function measure (gastric function, gastrointestinal inflammation, small intestines and pancreas, and colon), the majority of participants were within the low category for being priority. Cognitive measures means and ranges can also be found in Table 28.

Digit Symbol Substitution

For the first regression examining bowel function and Digit Symbol Subsitition , Model 1 was significant ($F(4, 103) = 4.896$, $p = .001$, $R^2 = .160$) with gender (B = -4.808, $SE_B = 2.216$, $p = .032$), age (B = -0.491, $SE_B = 0.185$, $p = .009$), and education (B = 5.380, $SE_B = 2.130$, $p = .013$) as significant predictors of the outcome variable, Digit Symbol Subsitition. Model 2 and Model 3 were non-significant adding no additional explained variance. Overall, being female, being younger, and having more years of education indicated better performance on the Digit Symbol Subsitition.

Identical Pictures

For the regression with the Identical Pictures cognitive measure, the first model was significant ($F(4, 103) = 7.211$, $p < .001$, $R^2 = 0.219$). Age (B = -0.75, $SE_B = 0.16$, $p < .001$) was the only significant predictor of the cognitive measure, Identical Pictures. The second and third model with the bowel function predictor variables were all non-significant, as well as the overall Model 2 and Model 3 significance.

Number Comparison

The fourth regression indicated a significant model 1 ($F(4, 103) = 4.2111$, $p = .007$, $R^2 = 0.141$, $p = .003$) with race (B = -9.134, $SE_B = 4.513$, $p = .046$), gender (B = -4.925, $SE_B = 1.892$, $p = .011$), and education (B = 3.950, $SE_B = 1.819$, $p = .032$) as significant predictors. This indicated that being white, female, and higher education was associated with better Number Comparison performance scores. Among Model 2 and Model 3 containing the bowel function predictors, there were no significant findings and no significant R_2 change.

AVLT

The first model in the regression for AVLT was statistically significant ($F(4, 103) = 4.178$, $p = .004$, $R^2 = 0.140$) with race (B = -2.875, $SE_B = 1.439$, $p = .048$), age (B = -0.103, $SE_B = 0.050$, $p = 0.044$), and education (B = -2.875, $SE_B = 1.439$, $p = .048$) as significant predictors. Model 2 was non-significant while Model 3 was ($F(4, 95) = 3.248$, $p = .015$, $R^2 = 0.264$) with the two quadratic predictors, gastrointestinal inflammation (B = -0.033, $SE_B = 0.017$, $p = .057$) and colon (B = 0.010, $SE_B = 0.005$, $p = 0.072$), being near significant. The curvilinear predictor of gastrointestinal inflammation indicated a significant relationship among AVLT performance and predictor scores of 7 and higher. Therefore, gastrointestinal inflammation scores above 7 were associated with worse AVLT immediate recall scores. The colon gastrointestinal curvilinear predictor indicated a slight dip in AVLT scores with moderate scores on the gastrointestinal measure. The initial overall model accounted for 14% of the variance and Model 3 added 10.1% additional variance to the overall model. Being younger, white, and having higher education indicated better performance on the AVLT, as well as a curvilinear relationship with the two

predictors, gastrointestinal inflammation and colon priority measures; see Table 29, Figure 13, and Figure 14.

Trails Making Test A

The regression model for the Trails Making Test as the outcome variable had no significant models indicated in Model 1, Model 2, or Model 3 and no significant predictors.

Trails Making Test B

Among the regression with Trails Making Test B as the outcome variable, Model 1 was significant ($F(4, 103) = 4.118$, $p = .004$, $R^2 = 0.138$). For Model 1, age (B = 0.006, $SE_B = 0.003$, $p = .048$) and education (B = -0.101, $SE_B = 0.032$, $p = .002$) were significant predictors of the Trail Making Test B. Model 2 and Model 3 provided no significant R^2 change to the overall model. Being younger and having higher education was related to better Trail Making Test B performance times.

AVLT Delayed

For the AVLT as the outcome variable among Model 1, race (B = -3.866, $SE_B = 1.436$, $p = .008$), gender (B = -1.883, $SE_B = 0.607$, $p = .002$), age (B = -0.109, $SE_B = 0.051$, $p = 0.034$), and education (B = 1.442, $SE_B = 0.579$, $p = .014$) were significant predictors. Model 1 overall was significant ($F(4, 102) = 6.543$, $p < .001$, $R^2 = 0.204$) while Model 2 was not. The Model 3 with the quadratic predictors was significant ($F(4, 94) = 2.974$, $p = .023$, $R^2 = 0.317$) adding 8.6% additional variance to the overall model for a total of 31.7% explained variance. The Gastrointestinal Inflammation quadratic preditor within Model 3 reached near significance (B = -

0.032, SE_B = 0.017, p = .067). This indicated that the gastrointestinal inflammation predictor had a negative association with AVLT Delay performance scores with predictor scores of 7 or more. This indicated that being white, female, younger, and higher education was related to better AVLT Delayed performance, as well as a curvilinear relationship among the quadratic predictor, gastrointestinal inflammation, and AVLT Delayed Performance; see Table 30 and Figure 15.

Digit Span Forward

For the Digit Span Forward as the outcome variable among Model 1, education (B = 0.929, SE_B = 0.427, p = .032) was the only significant predictor. Model 1 overall was significant (F(4, 103) = 2.827, p = .029, R^2 = 0.099) while Model 2 and Model 3 was not. This indicated that more education was related to better performance on the Digit Span Forward cognitive task.

Digit Span Backwards

The regression containing the Digit Span Backwards cognitive task as the outcome dependent variable resulted in non significant results in both Model 1, Model 2, and Model 3.

Category Fluency

The relationship among Category Fluency and bowel function was near significant (B = -0.256, SE_B = 0.122, p = .038), as well as an indication of a near significant curvilinear effect with the bowel predictor (B = -0.011, SE_B = 0.006, p = .072). Model 2 indicated that the bowel predictor, colon, was negatively associated with Category Fluency. Therefore, for every unit increase in the colon predictor, a -0.256 decrease in Category Fluency is predicted, holding all other variables. Only gender was significant in the initial controlled predictors indicating being

female was related to better category fluency performance (B = -2.204, SE_B = 1.057, p = .040). Model 1 overall was non-significant (F(4, 103) = 1.406, p = .237, R^2 = 0.052), but Model 2 (F(4, 99) = 2.326, p = .062, R^2 = 0.133) was near significant, as well as Model 3 including the quadratic bowel predictors (F(4, 95) = 2.298, p = .065, R^2 = 0.210). The curvilinear predictor, small intestines and pancreas, indicated a near significant relationship with Category Fluency performance scores. Scores approxiametly 15 and above on the small intestines and pancreas predictor was associated with lower Category Fluency scores. Although both model 2 and model 3 were only near significant at contributing an additional variance to the overall model, model 2 added 8.1% additional variance with Model 1 and Model 2 contributing 13.3% total variance and the quadratic (curvilinear predictors) added an additional 7.6% variance with the overall model being 21%; see Table 31, Figure 16, and Figure 17.

COWA

For the COWA task as the outcome variable among Model 1, education (B = 8.359, SE_B = 2.303, p < .001) was the only significant predictor. Model 1 overall was significant (F(4, 103) = 3.854, p = .006, R^2 = 0.130) while Model 2 was not. This indicated that more years in education was related to better performance on the COWA cognitive task.

Vocabulary

For the Vocabulary cognitive task as the outcome variable among Model 1, education (B = 4.083, SE_B = 1.378, p = .004) and race (B = -7.175, SE_B = 3.470, p = .038) were the only significant predictors. Model 1 overall was significant (F(4, 102) = 4.041, p = .004, R^2 = 0.137)

while Model 2 was not. This indicated that more education and being white was related to better performance on the Vocabulary cognitive task.

Question 3 summary

After each individual regression was ran separately with each cognitive domain as the outcome while controlling for age, ethnicity, gender, and education, the bowel measure was found to be a significant predictor for AVLT and AVLT Delay only. In both regressions that bowel function was a significant predictor, the overall model of the quadratic term of the predictor variable was significant while the linear term was not. Gastrointestinal inflammation had a negative association in both AVLT and AVLT Delay measures indicating lower scores in gastrointestinal inflammation resulted in better performance in AVLT and AVLT Delay, albeit after higher scores of the gastrointestinal inflammation bowel measure was reached, approxiamately scores seven and greater. The colon predictor for AVLT had a positive association indicating higher number on the colon bowel measure were associated with better AVLT scores, albeit a very small increase. The curvilinear associated indicated that AVLT scores decreased with colon bowel scores until colon bowel scores reached 12 and above. The regression with the category fluency measure as the outcome measure reached near significance with both the linear and quadratic model. Among the linear term, the colon predictor indicated lower scores were associated with better performance on the category fluency measure. The curvilinear relationship indicated higher scores on the small intestines and pancreas bowel measure were related to worse performance on the category fluency measure. The category fluency performance scores started dipping with scores of 15 and higher on the small intestines and pancreas bowel measure.

CHAPTER FIVE:

DISCUSSION

The purpose of the current study was to examine several different outcome measures; physical function, depression, and cognition, related to older adults. The outcome measures were chosen due to the increased risk of disability in older adults and to examine the moderating effect of bowel function with nutrients as a predictor based on prior findings related to the gut-brain-axis phenomenon (Brault, 2012; Heijtz et al., 2011). Since older adults are at a higher risk for malabsorption and nutrient deficiencies, it would be predicted that there is a moderating effect of bowel function in relation to these outcome measures, physical function and depression (Brownie, 2006). The current study helps identify the important moderating role that gut/bowel function may have on the physiological aspects of aging, as well as how gut/bowel function is related to cognitive performance in older adults. Within the first data set with participants 65 and older, the first question targets the relationship among nutrients and depression with fecal incontinence and Bristol Stool Form Scale that represents stool consistencies and transit times for digestion as moderators. The second question uses the same predictors and moderators, but the focus is on the outcome measure, physical function. Using a different data set, the Nutraceutical Blueberry Study, the third question uses a bowel questionnaire to investigate the association with several different cognitive domains in older adults.

By examining this relationship among different nutrient intakes and depression while looking at moderators, such as fecal incontinence, this gives us a step further into the interconnections of the biopsychosocial aspect of the broad influences of overall health. Results

of this study indicated some degree of bowel function influence within the questions asked in this particular older adult sample, as well as with immediate and delayed recall. This section will focus on the main findings within each question asked and explanatory results in accordance with the existing literature. Further, the limitations of the study, as well as the strengths will be followed along with a discussion of where this research area should be forthcoming in future studies.

Research question 1: Part A

Moderation of Fecal incontinence between Nutrient Components and Depression

Fecal incontinence can be a major life-altering phenomenon at any stage of one's life. The purpose of this question was to utilize the Bowel Health Questionnaire from the NHANES data as an indicative measure of a broad overall bowel health among older adults. Fecal incontinence has implications for symptoms of an unhealthy gut, as well as possible dysbiosis (Benno et al., 2016). The fecal incontinence measure was a significant moderator for Component 2 (fiber, calcium, phosphorus, magnesium, zinc, copper, and potassium), Component 3 (thiamin, riboflavin, niacin, vitamin B6, folate, folic acid, vitamin B12, and iron), Component 4 (total fat, vitamin E, sodium, MFA 18:1 (oleic), MFA 20:1 (eicosenoic), PFA 18:2 (linoleic), and PFA 18:3 (linolenic)), Component 5 (protein, cholesterol, choline, selenium, MFA 16:1 (palmitoleic), and PFA 20:4 (arachidonic)), Component 6 (alpha carotene, beta carotene, lutein, and vitamin K), Component 9 (carbohydrates, sugar, beta-cryptoxanthin, and vitamin C), Component 12 (alcohol), and vegetable intake with depression as the outcome. Among the significant components, the multivariate moderated regression indicated that Component 9 and Component 12 interaction with fecal incontinence was indicative of having the most influence when all

predictor variables were combined. Therefore, depending on the fecal incontinence score and the amount of carbohydrates, sugar, beta-cryptoxanthin, vitamin C, and alcohol largely influenced the outcome of depression compared to the other component nutrient predictor variables.

The main findings of the multivariate moderation regression analysis were the moderation of fecal incontinence between depression and the predictors: carbohydrates, sugar, beta-cryptoxanthin, vitamin C, alcohol, and vegetable intake. These will be the findings most elaborated on here. It is interesting to note that when examining low, moderate, and high fecal incontinence scores, the lower incontinence score had the lowest depression score but increased in depression with higher nutrients in Component 9. Although this is the case, it is important to note that where the moderation of fecal incontinence became significant were fecal incontinent scores of 3.056 or higher. The opposite was found for the moderate and higher incontinence scores as moderators with an increase in the nutrients from component 9 decreasing depression scores. Therefore, there were two different findings observed depending on the moderator, but the moderator value defining Johnson Neyman significant region would indicate to focus on the latter. It is also important to note that according to the findings in relation to alcohol and vegetable consumption, that those who had higher fecal incontinence scores, specifically 3.212 and above in the alcohol analyses and 1.783 and higher scores in relation to the vegetable analysis, would result in more benefits in decreasing depression scores. Therefore, suggesting an increase in low to moderate consumption of alcohol and higher vegetable intake among those with higher depression scores.

Carbohydrates can come in different forms, such as sucrose, fructose, and resistant starches. Component 9 included carbohydrates, as well as a sub-component of carbohydrates, sugar. There have been some negative and beneficial associations with carbohydrates found in

previous studies. Non-digestible carbohydrates are more so known for their benefits in gastric motility and help in regulating healthy bowel movements. Different than what was hypothesized, moderation of fecal incontinence with fiber, which was included in Component 2, and depression was only near significant. Carbohydrates can impact the circulation of hormones that influence satiety which may increase food intake (King, 2013). Looking at sugar, it has been found to possibly disrupt the signaling of satiety depending on the amount of consumption (Mitra et al., 2010). Therefore, these findings have been associated with sugar related to obesity and overeating (Dubois, Farmer, Girard, & Peterson, 2007; Miller, Niederpruem, Wallace, & Lindeman, 1994; Spruijt-Metz et al., 2009). However, there are still mixed results when it comes to sugar being the culprit for obesity, especially when compared to other factors, such as total fat and food processing (Crino, Sacks, Vandevijvere, Swinburn, & Neal, 2015; Ha et al., 2016; Stanhope, 2016). Sugar has also been known to have a connection with the brain processes that are associated with reward (Pelchat, 2002). The physiological response of sugar consumption may have helped increase calorie consumption when it was much needed when food was more scarce. With food more readily available in which is seen in the Westernized diet, this reward feedback tends to be a more go to for depressed individuals to compensate for those depressed feelings. Therefore, possibly causing a feedback loop that long-term results in other health issues, such as metabolic syndrome and obesity (Cordain et al., 2005; Whitaker, Sharpe, Wilcox, & Hutto, 2014). As for a different carbohydrate, resistant starches which are found in high carbohydrate foods, such as potatoes, and can avoid digestion in the small intestine have also been shown to impact colonic motility and possible fermentation as a result of short chain fatty acid conversion within the large intestine (Benno et al., 2016; Bird, Conlon, Christophersen, & Topping, 2010). Fecal incontinence can be a consequence of constipation due to the impact of

fecal matter and leakage (Romero, Evans, Fleming, & Phillips, 1996). It may be that having higher scores in fecal incontinence may indicate a disrupted gut microbiome, as well as issues with gut motility and uptake of carbohydrates. Increasing carbohydrates, broadly speaking, may help improve constipation and less likely to have a build-up leading to any leakage. Different carbohydrates very well contribute to energy sources for microbiota which may benefit the crosstalk among neurotransmitters, mobility, and muscle contractions (Trompette et al., 2014; Turnbaugh et al., 2009). Carbohydrates have also been shown to influence tryptophan that acts as a precursor to serotonin. When it comes to carbohydrate-rich foods, it may be more so the ratio of fats contained in that food and other additives that may determine whether the carbohydrates will have a positive impact on gut health (H. R. Lieberman, Caballero, & Finer, 1986).

Phytochemicals may be another avenue for functional foods and overall health. Beta-cryptoxanthin is a carotenoid that converts into vitamin A (Bauernfeind, 1972). Beta-cryptoxanthin is in many foods, such as foods containing wheat bran and many fruits (Zhou, Su, & Yu, 2004). As well as being known for a phytochemical, it is also well-known to have antioxidant properties (Young & Lowe, 2001). Within Component 9, increased amounts of beta-cryptoxanthin were shown to be related to lower depression scores, as well as lower depression in higher scores of fecal incontinence. In a study with older adult participants, depression was significantly higher in those who had lower amounts of cryptoxanthin, as well as vitamin C (Payne, Steck, George, & Steffens, 2012). Within the current study presented here, Component 9 also included vitamin C. Vitamin C is well-known for the vitamin's antioxidant properties (Bendich, Machlin, Scandurra, Burton, & Wayner, 1986). Vitamin C has also been shown to ameliorate depressive symptoms (Binfare, Rosa, Lobato, Santos, & Rodrigues, 2009). Additionally, vitamin C has been shown to be protective of gastric cancers (Waring et al., 1996).

Alcohol consumption examined as a predictor variable for depression was shown to be related to less depression with both low and high scores in fecal incontinence. Those with scores higher on the fecal incontinence scale were shown to have higher rates of depression but also the greatest decline in depression with increased alcohol intake. Recent studies have shown that low to moderate amounts of alcohol may be beneficial to your gut and your health (Cuskin et al., 2015; Lang, Guralnik, Wallace, & Melzer, 2007; Magalhaes, Carvalho, Cruz, Guido, & Barros, 2009; Mukamal et al., 2006). It may be the case between being low consumption of alcohol to chronic consumption, as well as what kind of alcohol it is. Red wine consumption has been shown to be beneficial to health due mostly to the polyphenols contained, in addition to the demonstration of benefiting the gut microbiota compositions, as well as improving health markers associated with metabolic disorders (Queipo-Ortuno et al., 2012). Studies have indicated that alcohol may have a regulation of bile acid formation that influences lipid metabolism and cholesterol utilization (Axelson, Mörk, & Sjövall, 1991; L. M. Nilsson et al., 2007). Bile acid is a metabolite that is dependent on the state of the gut microbiota (Ridlon, Kang, Hylemon, & Bajaj, 2014). In a study examining participants that were considered normal, having irritable bowel syndrome with diarrhea, and having irritable bowel syndrome with constipation, results indicated that there was an occurrence of malabsorption of bile acid excretion in those with the diarrhea symptoms (B. S. Wong et al., 2012). Therefore, depending on the fecal incontinence being due to constipation or diarrhea type symptoms, alcohol being associated with bile acid formation could help ameliorate constipation by acting as a laxative (Chey, Camilleri, Chang, Rikner, & Graffner, 2011; B. S. Wong et al., 2011). Interestingly, bile acid is an important key to digestive transit time, and therefore, could be influencing the absorption of nutrients and the gut microbiome. As with many things, there is most likely a homeostasis consideration to take in to account with too

much can cause other issues, such as being hard on your liver and gut (Engen, Green, Voigt, Forsyth, & Keshavarzian, 2015). In studies that involve, alcoholic fatty-liver disease, alcohol does impact the epithelial barrier of the gut in a negative way (Wood et al., 2013). If one is having issues with gut disturbances, it has been assumed that alcohol should be avoided (Konturek, Brzozowski, & Konturek, 2011). Within the current study, alcohol was shown to be related to lower depression scores in all ranges of fecal incontinence scores.

In relation to alcohol and mental well-being, there have been some positive findings with moderate consumption of alcohol being of benefit (Mortensen, Jensen, Sanders, & Reinisch, 2001). In a longitudinal study with women, it was found that moderate amounts were associated with lower rates of depression while demonstrating a possible protective effect (Gea et al., 2012). Suarez and colleagues found some interesting findings within their study exploring the relationship between depressive symptoms, alcohol, and C-reactive protein. Alcohol consumption was found to decrease C-reactive protein, which is related to inflammation, in those who had moderate to low scores in depression. With those having severe depression, this association was not found (Suarez, Schramm-Sapyta, Vann Hawkins, & Erkanli, 2013).

Vegetable intake has been well established to be beneficial to one's mental health (McMartin, Jacka, & Colman, 2013; Mihrshahi, Dobson, & Mishra, 2015). Vegetables can be high in many beneficial compounds, such as polyphenols and phytoestrogens (Pandey & Rizvi, 2009; Reverri, LaSalle, Franke, & Steinberg, 2015). Further, prebiotics which are resistant short-chain carbohydrates, are also found in specific vegetables (J. H. Cummings, Macfarlane, & Englyst, 2001). Although eating just vegetables alone is hard to obtain the same benefits of what is in a prebiotic supplement, the plant fiber has been shown to be benefit health (Slavin, 2013; Tungland & Meyer, 2002). For example, in mice specifically, brain-derived neurotrophic factor

(BDNF) was found to be increased with prebiotics via gut microbiota (Savignac et al., 2013). Depression has also been found to be higher in those who had lower vegetable consumption compared to those with higher vegetables in several meta-analyses (Lai et al., 2014; Tsai, Chang, & Chi, 2012). Not surprising, within this study, increased vegetable intake was related to decreased depression scores, and the higher the fecal incontinence score, the higher the depression scores. With an increase in vegetable amounts, the different amounts from low to high in fecal incontinence scores decreased depression scores.

Research question 1: Part B

Bristol Stool as a moderator between nutrient components and depression

The Bristol stool index is used as an indicator of bowel consistency and colonic transit time. Using the three categories, normal, constipation, and diarrhea, the moderating effects of these categorical groups were examined between nutrient components and depression. Constipation was found to be the significant categorical moderator in both Component 6 (alpha carotene, beta carotene, lutein, and vitamin K) and Component 11 (theobromine), albeit the overall model being only near significant. With Component 11 as a predictor, higher amounts of theobromine decreased depression in the constipation group. The opposite was found within the normal categorical group as a moderator indicating initial lower amounts of depression than the constipation group, but depression increased with increased amounts of theobromine. Interestingly, the different groups indicated differences in depression scores and how different nutrients may be influenced by the different types of bowel movements indicative of bowel transient times. Constipation may be an indicator or precursor of other health issues, such as metabolism. Faulty metabolism may be an issue due to important metabolites not able to be

produced, such as short-chain fatty acids (Tremaroli & Backhed, 2012). These metabolites are important for health, such as energy for cellular processes, signaling hormones, and bile acid activity (Thomas, Pellicciari, Pruzanski, Auwerx, & Schoonjans, 2008). Therefore, this would lead to issues that regulate the mucosal immune system that may lead to age-related physical problems (Maslowski et al., 2009). Alpha carotene, beta carotene, and lutein are all considered antioxidants. Studies involving depression have been shown to be associated with the number of antioxidants and the rate of depression (Gautam et al., 2012; Park, You, & Chang, 2010; Payne et al., 2012). Antioxidants have been shown to decrease oxidative stress, that, therefore, decreases inflammation and stress related markers in the body (Halliwell, 1989). Considering the aging population, there has also been evidence of a compromised colonic dysfunction with elevated free radicals (Conner, Brand, Davis, Kang, & Grisham, 1996). Theobromine, mostly known for being in chocolate, has mixed results when it comes to impacting mood and depression. Within a study with healthy adults, theobromine did not improve mood, although the mood measurement was not related to depression (Judelson et al., 2013). In another study examining mood in healthy participants, a dose-dependent relationship was found with theobromine. Higher amounts had no benefit on mood, but there was a small improvement in mood with low to moderate amounts of theobromine (Baggott et al., 2013). Among a study that measured mood and mental calmness, mental calmness increased with the consumption of theobromine, as well as helped with blood pressure (E. S. Mitchell et al., 2011). It may also be noted that there has been evidence of the type of stool correlating with transit time, as well as microbial diversity and/or richness (Vandeputte et al., 2015). Many studies have connected microbial richness with a healthy microbiome, but Roager and colleagues (2016) found that faster transit time was related to improving the colonic mucosa, albeit less microbial richness.

Research question 2: Part A

Moderation of Fecal incontinence between Nutrient Components and Physical Function

Question 2 examined fecal incontinence as a moderator between nutrients and physical function. There were no significant findings involving moderation within the current study. Although there were no significant moderation relationships indicated, the fecal incontinence measure was significantly related to physical function. Component 5 (alpha carotene, beta carotene, beta-cryptoxanthin, lutein, vitamin C, and vitamin K) and Component 6 (MFA22_1, PFA18_4, PFA20_5, PFA22_5, and PFA22_6) were also significant predictors for physical function, as well as Component 10 (lycopene) being near significant (p = .074). The lack of findings were somewhat surprising due to nutrient intake being related to physical function in prior studies, as well as fecal incontinence being shown to significantly contribute to problems with the quality of life and physical function (Ouslander, Zarit, Orr, & Muira, 1990; Rothbarth et al., 2001). Being an older adult population within this current sample and how common bowel issues are, it was also suspected that fecal incontinence as a moderator might be more pronounced (Camilleri, Lee, Viramontes, Bharucha, & Tangalos, 2000). Another factor that may have impacted the findings is that the sample was mostly healthy without indication of disability, as well as not very robust scores in fecal incontinence.

Research question 2: Part B

Bristol Stool as a moderator between nutrient components and physical function

Bristol stool function was examined as a moderator between nutrients and physical function. Among the different nutrient components, Component 6 (MFA22_1/ Euric acid,

PFA18_4/stearidonic acid, PFA20_5/EPA/Timnodonic acid, PFA22_5/DPA/Clupanodonic acid, and PFA22_6/DHA/Cervonic acid) with Bristol Stool as a moderator was significant and Component 9 (vitamin A and retinol) as a predictor and the moderator were near significant. Among the Bristol Stool categories, constipation had poorer physical function than the diarrhea group. Both groups improved in physical function with more nutrients in Component 6. Within Component 9, only the constipation category from the Bristol Stool was near significant. Surprisingly, there was an inverse relationshipbetween vitamin A and retinol indicating higher amounts of vitamin A and retinol resulting in worse physical function.

Component 6 consisted of mostly omega-3 fatty acids which have been found to be anti-inflammatory in many studies. Additionally, the Western diet is known to be higher in omega-6 fatty acids which have had many theorize the possible issues we see with health problems (A. P. Simopoulos, 2002). Further, Omega 3s have been shown to be beneficial to Crohn's disease and ulcerative colitis with less relapse and less use of corticosteroids (Aslan & Triadafilopoulos, 1992; Hawthorne et al., 1992; Lorenz et al., 1989). In a study exploring rectal cell proliferation, the ratio of omega 6s and omega 3s associated with different diets was compared. Results demonstrated that fish oils high in omega 3s were dependent on the initial type of diet based on omega ratio to be beneficial for rectal cell proliferation (Bartram et al., 1995). In the current study, there was worse physical function in those that were constipated, but an increase in these nutrient components improved physical function in both the constipated group and diarrhea group. The constipation category indicated having more influence with the addition of the nutrients than the diarrhea category. With previous findings on the beneficial effects of omega 3s on overall health and cellular proliferation associated with the gut, the results indicate the

importance that these polyunsaturated fatty acids have in obtaining healthy bowel health and physical function.

Vitamin A and retinol were near significantly associated with physical function and the Bristol stool category, constipation, as a moderator. Interestingly, the association indicated that more vitamin A resulted in worse physical function in those with constipation. Although vitamin A has an important role in an individual, there are some negative findings found with vitamin A that may help explain the results that were found in this current study. In a study that included mid and old-aged women from Sweden, increased retinol intake was associated with decreased bone mineral density (Melhus et al., 1998). An issue with vitamin A may be the overabundance of the vitamin in developed countries (Allen & Haskell, 2002). Within the current study, constipation was the category indicative of being a moderator among physical function and vitamin A and retinol. Since constipation is known to have a longer transit time involved with the gut, it may be that there is more vitamin A being absorbed or influencing other mechanisms than if one had a normal bowel or diarrhea. The quality of absorption could be an important implication in how the digestive system can moderate the relationship between vitamin A and physical function, especially with older adults being at higher risk for osteoporosis and falls (S. R. Cummings & Melton, 2002; Verma et al., 2016).

Research question 3

Is there a relationship among gut health and cognitive performance?

Within research question 3, the Nutraceutical Blueberry Study data was used to examine multiple cognitive domains and gut disturbances on different priority scales. Significant results were only found among the AVLT immediate recall with curvilinear predictors, gastrointestinal

inflammation and colon, and AVLT Delay recall with curvilinear predictor, gastrointestinal inflammation. The curvilinear relationship among AVLT immediate recall and the gastrointestinal inflammation bowel predictor, which is one of the four categories in the bowel questionnaire, indicated that with increased scores on the bowel predictor of seven and higher indicated lower scores on the AVLT. Interestingly, the curvilinear relationship with the colon bowel predictor indicated that low to moderate scores was related to lower AVLT scores while moderately high to higher scores for the colon bowel predictor was related to slightly higher AVLT scores, albeit resulting in very little change on the AVLT. The AVLT delayed curvilinear relationship with the gastrointestinal inflammation bowel predictor was similar to what was described previously with AVLT immediate recall with lower scores on the bowel predictor being related to higher AVLT Delayed scores while moderate to high scores on the bowel predictor was related to lower AVLT Delayed scores. There was a near significant overall model with Category Fluency and the linear predictor, colon, and the curvilinear predictor, small intestines and pancreas. The linear colon bowel predictor indicated higher scores were related to lower scores on the Category Fluency measure. With the near significant curvilinear small intestines and pancreas bowel predictor, the relationship indicated higher scores on the bowel predictor indicated lower scores on the category fluency, while very low scores on this bowel predictor was related to only slightly higher scores on the category fluency measure.

In a study be Castaneda and colleagues (2013), similar results in relation to verbal learning was found among a group of adolescents experiencing irritable bowel disease compared to the control group. Such findings are interesting because within the current study, several cognitive measures were administered with only verbal learning being significantly related to our gut outcome measure. Kennedy and colleagues have also found a relationship between cognition

and IBS, albeit different than IBD. Several cognitive measures were administered, albeit no verbal learning measure, indicated a relationship with visuospatial memory (Kennedy et al., 2014). Another study that contained participants with IBS and IBD found significance in verbal IQ as measured by the Wechsler Abbreviated Scale of Intelligence compared to a healthy control group (Attree, Dancey, Keeling, & Wilson, 2003). In additional support for the brain-gut-brain axis, Aizawa and colleagues (2012) examined a small sample of participants with IBS and a control group. With the supplementation of functional magnetic resonance imaging (MRI) along with measuring cognitive flexibility, there was a significant difference among the two groups that indicated decreased brain activity and cognitive flexibility. In another study that used MRI to examine the gray matter, there was an indication of decreased gray matter in several areas of the brain that relate to attention moderation separate from the emotional area for brain activity compared to the control group (Seminowicz et al., 2010). As for other cognitive tasks not being related, it may be that more was not found due to the participants being in mostly the healthy range and not showing higher levels of gut disturbances. Associations may not be indicative unless there are more extreme gut disturbances. Additionally, these were older adults that were still cognitively healthy that was required to pass the screening process. Additionally, the bowel questionnaire has not been validated.

The results are hard to compare due to lack of research in this area, particularly with specific cognitive functions. The brain-gut-axis in the aging population has many implications for therapeutic targets. There is evidence of neurotransmitter depletion in older adults with cognitive aging disorders, as well as micro-organisms that may contribute to brain function (Afifi, Jiman-Fatani, Tonkal, & Jamjoom, 2016; Backman et al., 2000). This relationship of neuron depletion in the central nervous system (CNS) may also be a contributing factor in the gut

with gut neuronal maintenance, such as neural crest stem cells and 5-HT receptors related to serotonin (Camilleri, Cowen, & Koch, 2008; Fiorica-Howells, Maroteaux, & Gershon, 2000). Gut motility and many of the impacts that you may see on a gut questionnaire given, such as colon inflammation, may be a consequence of direct impact with these neural functions in the ENS and CNS cross-talk (Kruger et al., 2002; Singaram et al., 1995). This has led to several theories involving mental health disorders, such as schizophrenia. The neurotransmitter theory may be an avenue that gives enough evidence and speculation of the cross-talk and inter-relationships of the whole body process with the gut and the brain. This theory concentrates on several different neurotransmitters that are found in the gut, such as dopamine and serotonin (J. A. Lieberman et al., 1998). Speculation that the current state of the gut may be an indicator or related to cognition, especially in older adults with gut changes related to aging, has led to examining the several inter-relationships with the bowel and brain relationship. Additionally, having evidence of mental health being associated with the microbiome, it would be safe to speculate that this may, as well, have an impact on cognitive function. Evidence of inflammation in the aging process also supports this idea of stress impacting both the gut and the brain and the bidirectional relationship (Cebra, 1999; E. Clark, Hoare, Tanianis-Hughes, Carlson, & Warhurst, 2005; Emilio, Felicita, & Thea, 2012; Sparkman & Johnson, 2008). This may be indicative of the top-down process of the brain influencing the gut. There is supportive evidence that stress and emotions from negative life events may cause dysregulation in cognitive function due to arousal that we may or may not be consciously aware of (Brosschot, Gerin, & Thayer, 2006). There has been indication of these outside stressors perturbing the regulation of the prefrontal cortex, hippocampus, and amygdala by emotional events or the activation of the fight or flight response (Sherin & Nemeroff, 2011). Therefore, this may result in physiological reactions, such as stress-

related hormones, associated with the gut that may further result in “gut reactions”. These neuronal signals from the brain may influence disruption in the gastrointestinal system via the vagus nerve causing dysregulation in bowel emptying and gastrointestinal upset. This leads to a perpetual cycle of the negative influences of the bi-directional relationship among the gut-brain axis (Eriksson, Andren, Kurlberg, & Eriksson, 2015). Further, in relation to different areas of the gut, the colon has been found to have transit slowed compared to other areas of the digestive tract (Y. T. Wang et al., 2015). Therefore, the colon is dense with bacteria in comparison and, therefore, can result in fermentation (Nyangale, Mottram, & Gibson, 2012). It is not yet known how fermentation of bi-products in the gut may impact cognition by indirect or direct pathways to the brain (i.e. the vagus nerve). Further, fermentation in the colon has been related to beneficial metabolites, such as short-chain fatty acids and butyrate, that are related to polyunsaturated fatty acid consumption (Kolar et al., 2007; J. M. Wong, de Souza, Kendall, Emam, & Jenkins, 2006). Both polyunsaturated fatty acids and these metabolites have been shown to be important to cognitive function as indicated in several studies involving older adults (A. Nilsson, Radeborg, Salo, & Bjorck, 2012; Witte et al., 2014; Yurko-Mauro et al., 2010). The colon is often a site where bowel disorders are recognized and may be a viable target for cognition with further investigation of the gut-brain axis. In participants with irritable bowel syndrome, there is also an indication of cognitive disruption in the hippocampus. The tryptophan and kynurenine activity has been shown to be an important regulator for cognitive performance in IBS. A study by Kennedy and colleagues (2015) found that elevated levels of tryptophan and kynurenine were elevated in those with IBS, and visuospatial episodic memory performance was significantly impacted compared to healthy controls. Such findings have led to hypothesize that those with gut disturbances may not metabolize these important amino acids the same as normal

bowel functioning individuals that lead to different metabolite processes (Kennedy et al., 2015). The conversion of metabolites has been shown to rely on gut microbiota, specifically tryptophan, as demonstrated with mice (Clarke et al., 2013). This also leads to the role of serotonin levels in play with the gut and the impact on cognitive status (Buhot, Martin, & Segu, 2000). Studies have also demonstrated cognitive performance deficits in memory within mice that were lacking established gut bacteria. Probiotics also helped attenuate this dysfunction in memory when administered and compared to control mice. This has drawn another bridge between influences on hippocampal processes and the importance of an intact gut microbiome (Gareau et al., 2010).

Strengths

There are several strengths to the current study presented. With the use of two data sets, there is the ability to target several questions in relation to the gut-brain-axis. Within the first data set, the NHANES is population-based and contains an extensive dietary nutrient intake, as well as medication and supplement use. Although the dietary nutrient intake is based off a 24-hour recall food frequency questionnaire, having an additive second 24-hour recall administered and assessed using the Automated Multiple-Pass Method developed by the USDA is purposely used to examine variation that may occur. Dietary data collection can be controversial in the use of certain methods, but the USDA's part in the estimates of dietary intake minimizes the inaccuracy of the data by thoroughly checking for errors.

The NHANES also has two different gut questionnaires that target two issues, fecal incontinence and transit time. Fecal incontinence is a condition shown to be NHANES also has a large data set that even after taking out several participants that did not have all the measures cited, there was a large sample size. In the Blueberry Nutraceutical Study data set, there is an

extensive amount of cognitive measures that examine several different cognitive domains. The Nutraceutical Blueberry Study had many strengths pertaining to the cognitive performance measures. The cognitive measures used have been validated and are reliable measures. Secondly, the administration of several cognitive performance measures did not limit the current study's findings to one cognitive domain. Additionally, the gut assessment is an extensive questionnaire targeting several areas of broadly related to the gut. Additionally, having access to an older adult sample in both data sets allows me to have access to an understudied area related to diet, gut/bowel function, physical function, cognition, and mental well-being.

Limitations

Taken into account all the strengths of the study, there are several limitations that must be addressed. Within the NHANES, the measures were all self-reported which may result in response bias. Additionally, there are no blood values to assess nutrient intake, as in the previous NHANES data sets before 1999. Although this is the case, experts in the field that are knowledgeable on dietary intake measurement practices have come to a consensus on the dietary methods used in the NHANES (Wright, Ervin, & Briefel, 1994). It must also be acknowledged that although the NHANES procedure for dietary intake is proceeded to obtain the least bias in the data, there is always the possibility of bias to still occur. There is also the issue of underreporting energy intake that has been previously recognized. Unfortunately, to correct this issue within the NHANES data, it would most likely lead to several other issues, such as attrition and impracticality of the overall assessment of the study (Ahluwalia, Dwyer, Terry, Moshfegh, & Johnson, 2016). Also, it must be remembered that the nutrient intake was based on conversions of the daily food intake reports and the estimate of nutrients for that intake for each

participant. While looking at the gut, it should be recognized that nutrients that are absorbed may be different than what is consumed initially. Also, depending on the state of the gut microbiota and diet of the individual, that actual nutrient absorption may be different.

The gut measures are also limited to fecal incontinence and the Bristol Stool Form Scale within the NHANES data. Although both useful measures while looking at the relationship of gut/bowel function as a moderator, there were no measures of gut microbiota to supplement these measures or specific metabolite data. Although, the Bristol Stool Form Scale has had recent studies to support the measure being significantly corresponding to specific gut microbiota and transit times related to microbiota richness (Hadizadeh et al., 2016; Tigchelaar et al., 2015). Further, the subjects used were non-institutionalized. Therefore, scores may be lower than what would be found if the participants were. Within the Nutraceutical Blueberry Study, the gut questionnaire has not been validated and has been used more so as a screener in clinics. Therefore, the measure has not been thoroughly used in prior studies and lacks the ability for any form of comparative analysis. Additionally, the sample used was a healthy cognitive sample and non-institutionalized. Within both data sets, the data was self-report, as well as non-longitudinal.

As for the two outcome measures used with the NHANES data, depression and physical function, both were self-reported measures. Again, self-reported measures can lead to biased results and would benefit to be combined using performance measures and psychological assessment by a professional.

An additional limitation with the second data set is that the participants were screened for any indication of problems with cognitive performance using the Mini-Mental State

Examination. For future studies, it would be interesting to get a broader range of cognitive scores that may increase the likelihood of finding a more pronounced relationship with bowel function.

Future research

The research among the gastrointestinal field has had some astounding findings that hold many promises for future therapeutic interventions, but the specific mechanisms have yet to be fully determined. To move this field of study forward, more investigational, long-term human studies are needed, although, animal studies have provided an important basis to continue on. Probiotics and prebiotics have been suspected to be a powerful tool when it comes to assisting beneficial gut microbiota and maintaining healthy gut function, therefore, deserving further attention. Different foods and the diversity of food intake also needs to be further investigated. There are many discrepancies in the different types of food and the health/risk benefits. For example, fats were given a bad reputation for contributing to diabetes and cardiovascular diseases. Now, recent research is finding that it may not be a large culprit in these health conditions and may be beneficial, albeit certain types of dietary fats (Estruch et al., 2016; Praagman et al., 2016; D. D. Wang et al., 2016). Another recent study focused on how certain foods that are mostly known to be good for you may not be so beneficial to someone else (Zeevi et al., 2015). By focusing more so on potential moderators and what may fluctuate the benefits or risks of such diets may make using functional foods in a clinical setting more realistic. Functional foods could be used to manipulate the gut to increase beneficial metabolites, such as short-chain fatty acids and butyrate. Clarity is also needed with how the diet may impact the gut, as well as issues related to overall health in the aging population. By grasping a further understanding of the natural aging process of the gut, this may provide what direction we need to

focus on next to be preventative or how to provide effect therapy. If inflammation is largely the cause of many of the issues examined within the aging population and gut disturbances, finding specific mechanisms that may lessen the impact of inflammation and in turn, help with the immune system could be a viable target.

CHAPTER SIX:

CONCLUSION

The interest in the gut microbiome and overall health has increased substantially over the last several years indicating to be an important target for interventions and the clinic. Therefore, it seems like a viable area of study to initiate further research with the older adult population. The current study indicates that bowel function may be a viable target for interventions and prevention when it comes to older adults' health associated with nutrition, depression, physical function, and cognition.With the ever-increasing older adult population, different bowel measures may be a cost-effective and easily accessible way to prevent or determine whether more substantial measures are needed. Further, more research is needed to properly know if this is an effective alternative to more invasive measures and what steps are needed to improve gut health in older adults. This study adds to the evidence that bowel health, albeit indicated by self-reported measures, deserves further attention in supporting older adults and their health.

Saturated Fatty Acids	Butanoic SFA 4:0
	Hexanoic SFA 6:0
	Octanoic SFA 8:0
	Decanoic SFA 10:0
	Dodecanoic SFA 12:0
	Tetradecanoic SFA 14:0
	Hexadecanoic SFA 16:0
	Octadecanoic SFA 18:0
Polyunsaturated Fatty Acids	Octadecadienoic PFA18:3
	Octadecatetraenoic PFA 18:4
	Eicosatetraenoic PFA 20:4
	Eicosapentaenoic PFA 20:5
	Docosapentaenoic PFA 22:5
	Docosahexaenoic PFA 22:6
Monounsaturated Fatty Acids	Hexadecenoic MFA 16:1
	Octadecenoic MFA 18:1
	Eicosenoic MFA 20:1
	Docosenoic MFA 22:1

Figure 1: List of Unsaturated Fatty Acids

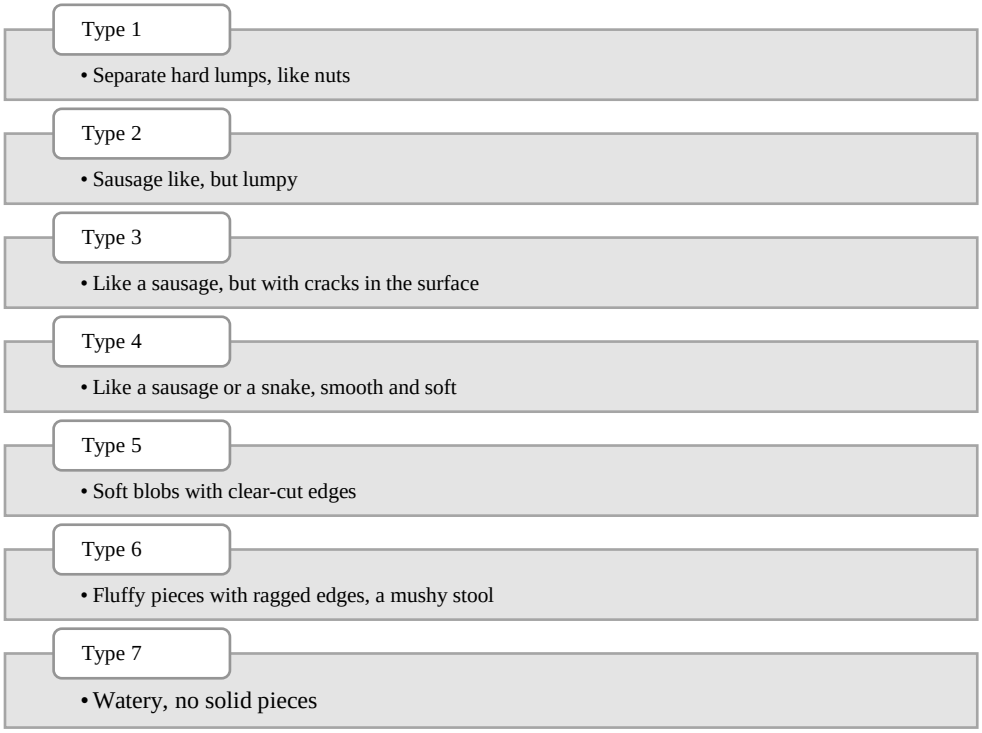

Figure 2: Bristol Stool Form Scale Types and Descriptions

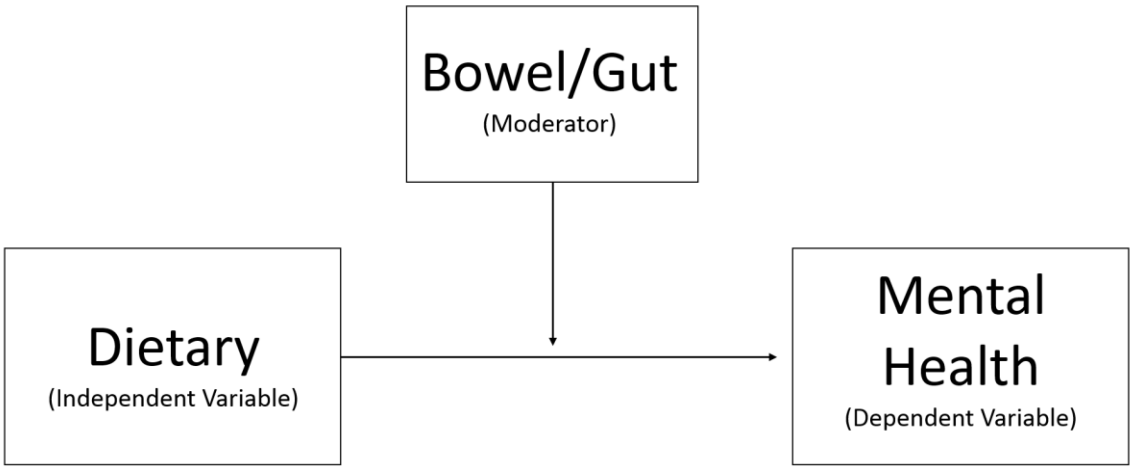

Figure 3: Question 1 Diagram of Bowel Function as a Moderator among Diet and Depression

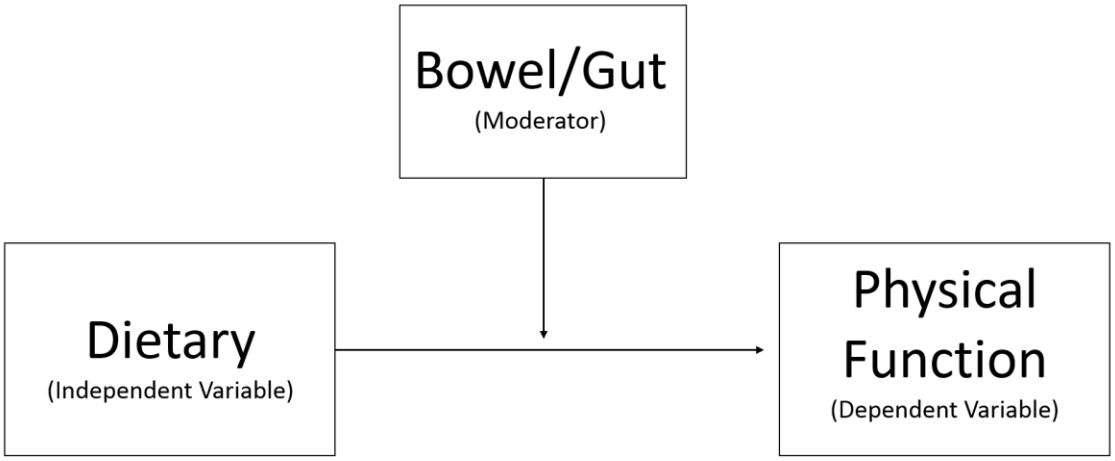

Figure 4: Question 2 Diagram of Bowel Function as a Moderator among Diet and Physical Function

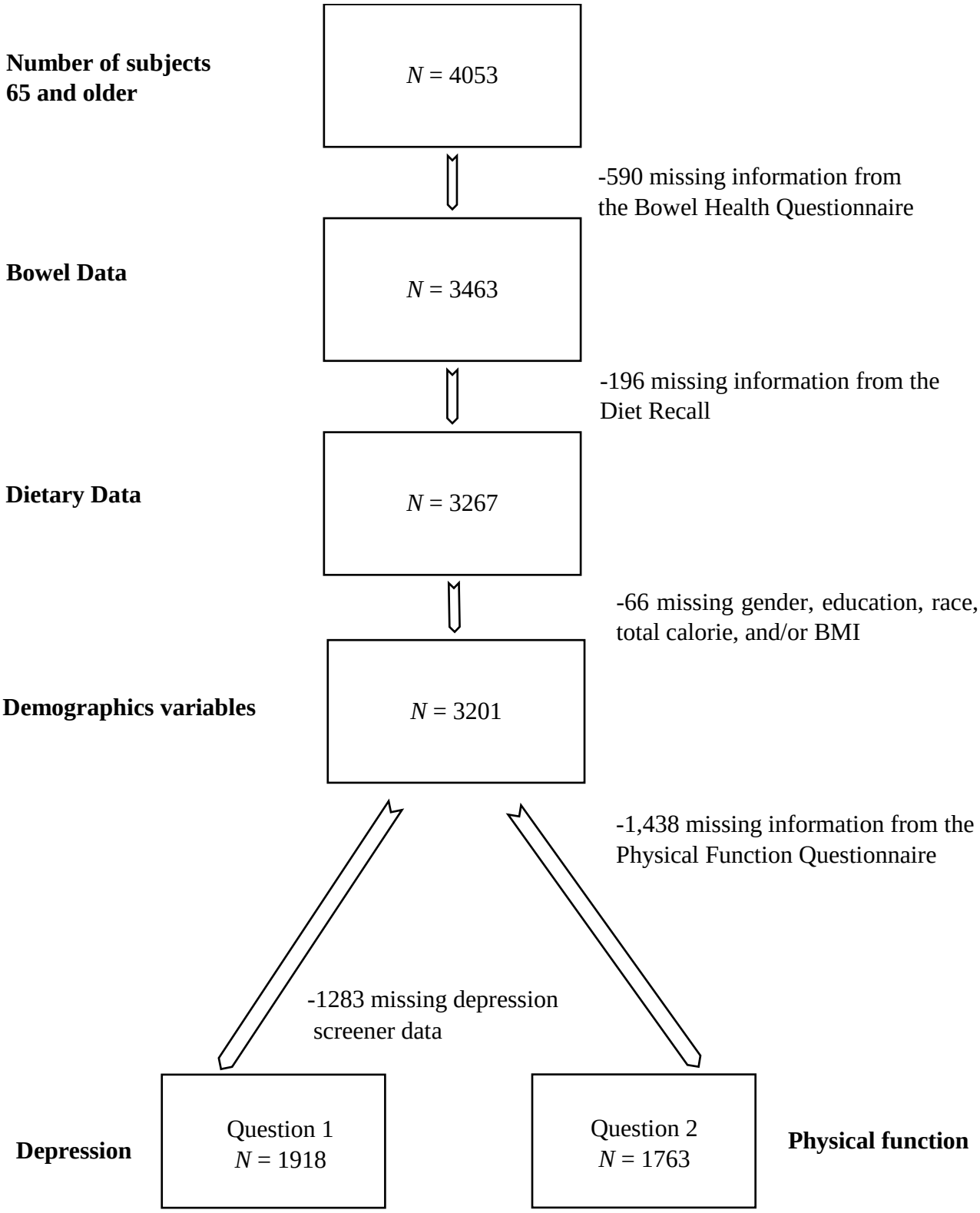

Figure 5. Flowchart of participants for the analytic sample

Table 1**:** Demographic Characteristics for Depression Analytic Sample in the National Health and Nutrition Examination Study

Characteristic	All *N* = 1918	
	M (%)	*SD*
Age (y)	73.76	5.55
Depression	3.85	3.85
Fecal Incontinence	3.04	2.47
Ethnicity (white)	(66.5)	
Gender (female)	(56.3)	
Education		
less than ninth grade	(18.6)	
9-11 education	(17.8)	
High School graduate/GED	(27.0)	
some college or associates degree	(20.6)	
college graduate or above	(16.0)	
Physically Active	(54.4)	
Overweight	(26.5)	
Supplement Use	(37.5)	
Antacid Use	(7.8)	
Special Diet	(68.6)	
Prescription Drug Use	(19.4)	
Bowel Normality	(73.4)	
Constipation	(8.20)	
Diarrhea or Urgency	(17.1)	

Note. Possible depression scores ranged from 0-30; possible fecal incontinence scores ranged from 1-20.

Table 2: Dietary Characteristics for Depression Analytic Sample in the National Health and Nutrition Examination Study

	N = 1918				
Characteristic	*M*	*SD*	Characteristic	*M*	*SD*
Niacin (mg)	19.87	9.75	Energy (kcal)	1646.94	576.35
Folate (mcg)	183.50	96.49	Protein (gm)	64.84	28.03
Folic Acid (mcg)	162.92	143.54	Carbohydrate (gm)	205.56	79.54
Iron (mg)	13.60	7.18	Total sugars (gm)	92.23	51.58
Vitamin B6 (mg)	1.71	1.02	Dietary fiber (gm)	15.04	8.07
Cholesterol (mg)	239.73	190.24	Lycopene (mcg)	4265.08	7751.08
Choline (mg)	279.22	141.68	Meat (gm)	19.98	50.65
Phosphorus (mg)	1095.69	444.98	Vegetable (gm)	178.35	188.47
Sodium (mg)	2726.39	1215.73	Coffee (gm)	1541.21	970.51
Selenium (mcg)	87.54	42.54	Sugar (gm)	20.20	43.65
Total Fat (gm)	62.23	29.28			
Vitamin E (mg)	6.31	4.20			
Alpha Carotene (mcg)	441.49	972.98			
Beta Carotene (mcg)	2259.45	3361.34			
Lutein (mcg)	1455.68	3002.73			
Vitamin K (mcg)	95.76	154.10			
Retinol (mcg)	428.75	577.03			
Riboflavin (mg)	1.90	0.92			
Calcium (mg)	790.11	450.54			
Vitamin B12 (mcg)	4.71	6.47			
Vitamin A (mcg)	639.86	655.29			
Beta-cryptoxanthin (mcg)	110.43	253.62			
Vitamin C (mg)	81.25	77.68			
Magnesium (mg)	251.38	107.71			
Potassium (mg)	2415.68	1006.84			
Theobromine (mg)	30.61	59.07			
Copper (mg)	1.17	1.10			

Table 3: Fatty Acid Characteristics for Depression Analytic Sample in the National Health and Nutrition Examination Study

	N = 1918	
Characteristic	*M* (%)	*SD*
Saturated Fatty Acids (gm)	20.53	11.04
SFA 4:0 (Butanoic) (gm)	0.43	0.43
SFA 6:0 (Hexanoic)	0.24	0.25
SFA 8:0 (Octanoic)	0.20	0.22
SFA 10:0 (Decanoic)	0.36	0.34
SFA 12:0 (Dodecanoic)	0.66	1.09
SFA 14:0 (Tetradecanoic)	1.70	1.36
SFA 16:0 (Hexadecanoic)	11.04	5.56
SFA 18:0 (Octadecanoic)	5.28	2.83
Monounsaturated Fatty Acids (gm)	22.68	11.57
MFA 16:1 (Hexadecenoic)	0.93	0.64
MFA 18:1 (Octadecenoic)	21.26	10.93
MFA 20:1 (Eicosenoic)	0.2	0.17
MFA 22:1 (Docosenoic)	0.02	0.08
Polyunsaturated Fatty Acids (gm)	13.61	7.81
PFA 18:3 (Octadecatrienoic)	1.26	0.94
PFA 18:4 (Octadecatetraenoic)	0.01	0.03
PFA 20:4 (Eicosatentaenoic)	0.11	0.11
PFA 20:5 (Eicosapentaenoic)	0.03	0.1
PFA 22:5 (Docosapentaenoic)	0.02	0.03
PFA 22:6 (Docosahexaenoic)	0.06	0.15

Table 4: Bowel Characteristics for Depression Analytic Sample in the NHANES

N = 1918

Characteristic	*n*	%
Common Stool Type		
Type 1 (separate hard lumps, like nuts)	56	2.9
Type 2 (sausage-like, but lumpy)	103	5.3
Type 3 (like sausage but with cracks in the surface)	403	20.8
Type 4 (like sausage or snake, smooth and soft)	1023	52.7
Type 5 (soft blobs with clear-cut edges)	161	8.3
Type 6 (fluffy pieces with ragged edges, a mushy stool)	172	8.9
Type 7 (watery, no solid pieces)	24	1.2

Table 5: Pearson Correlation Coefficients among Demographic Variables and Depression

	Depression	Bowel
Age	-0.059*	-0.024
Ethnicity	-0.088***	0.083***
Female	0.039†	0.018
Education	-0.104***	0.041†
BMI	0.033	-0.013
Physical Activity	-0.135***	0.022
Calories	-0.083***	0.064**
Supplement Use	0.014	-0.002
Antacid Use	-0.020	-0.001
Special Diet	0.062**	0.054*
Prescription Drug Use	0.012	-0.002

***p<.001, **p<.001, *p<.05, †p<.10

Table 6. Pearson Correlation Coefficients among Demographic Variables and Dietary Measures

	Age	Ethnicity	Female	Education	BMI	Physical Activity	Calories	Suppl. Use	Antacid Use	Special Diet	Rx Use
Protein	-0.076**	0.097***	0.265***	0.122***	0.011	0.112***	0.762***	-0.019	0.050*	-0.015	0.011
Carbohydrates	0.006	0.087***	-0.184***	0.107***	-0.071**	0.074**	0.844***	0.000	0.011	-0.018	-0.004
Sugars	0.037	0.096***	-0.104***	0.097***	-0.058*	0.068**	0.631***	-0.015	-0.014	-0.050*	-0.010
Fiber	0.009	0.098***	-0.096	0.196***	-0.081***	0.144***	0.549***	0.016	0.011	0.088***	-0.020
Total Fat	-0.058*	0.182***	-0.232***	0.069**	-0.001	0.071**	0.835***	-0.013	0.033	-0.063**	0.029
Cholesterol	-0.080***	0.060**	-0.208***	0.002	0.040†	0.027	0.488***	-0.018	0.044†	-0.049*	0.024
Vitamin E	0.009	0.201***	-0.133	0.146***	-0.028	0.128***	0.602***	0.000	0.044†	-0.005	0.011
Vitamin A	0.066**	0.206***	-0.062**	0.106***	-0.027	0.068**	0.388***	0.001	0.007	0.052*	0.000
Alpha Carotene	0.010	0.067**	0.009	0.123***	-0.015	0.065**	0.137***	0.002	0.012	0.033	-0.028
Beta Carotene	0.041†	0.095***	-0.002	0.134***	-0.050*	0.092***	0.220***	0.001	0.017	0.024	0.007
Beta Cryptoxanthin	0.075**	0.036	-0.019	0.110***	0.00	0.055*	0.204***	0.001	-0.031	0.014	0.010
Lycopene	-0.047*	0.064**	0.025	0.087***	0.011	0.037	0.152***	-0.011	0.011	0.017	0.044†
Lutein	0.031	0.095***	-0.047*	0.137***	-0.068**	0.093***	0.251***	-0.023	0.002	0.032	0.011
Thiamin	0.043†	0.179**	-0.224	0.120***	-0.016	0.064**	0.629***	-0.022	0.004	0.021	0.000
Riboflavin	0.008	0.262***	-0.217	0.122***	0.022	0.086***	0.609***	-0.020	-0.001	0.037†	-0.001
Niacin	-0.010	0.161***	-0.235***	0.120***	-0.001	0.097***	0.638***	-0.001	0.050*	0.004	0.014
Vitamin B6	0.019	0.166***	-0.199***	0.135***	0.002	0.099***	0.554***	0.002	0.035	0.017	-0.022
Folate	0.032	0.176***	-0.149***	0.139***	-0.024	0.087***	0.574***	-0.008	0.026	0.034	-0.008
Folic Acid	0.086***	0.139***	-0.077**	0.053*	0.008	0.014	0.351***	-0.008	0.032	0.018	-0.005
Retinol	0.088***	0.239***	-0.062**	0.083***	0.009	0.045*	0.407***	0.001	-0.001	0.045*	-0.002
Choline	-0.064**	0.116***	-0.275***	0.079**	0.018	0.101***	0.672***	-0.017	0.040†	-0.025	0.021
Vitamin B12	0.015	0.204***	-0.160***	0.083***	0.020	0.062***	0.435***	0.023	0.011	0.021	-0.013
Vitamin C	0.060**	0.069**	-0.036	0.162***	-0.003	0.101***	0.287***	-0.030	-0.025	0.042†	-0.031
Vitamin K	-0.012	0.077**	-0.020	0.111***	-0.048*	0.105***	0.335***	-0.018	0.021	0.046*	0.006
Calcium	-0.022	0.171***	-0.096***	0.124***	0.006	0.055*	0.562***	-0.004	0.021	0.041†	-0.015
Phosphorus	-0.046*	0.180***	-0.237***	0.138***	-0.005	0.112***	0.797***	-0.015	0.029	0.033	0.010
Magnesium	-0.037	0.146***	-0.176***	0.190***	-0.045*	0.154***	0.728***	0.002	-0.001	0.061**	0.016

Table 6: Contd.	Age	Ethnicity	Female	Education	BMI	Physical Activity	Calories	Suppl. Use	Antacid Use	Special Diet	Rx Use
Iron	0.033	0.178***	-0.207***	0.115***	-0.005	0.089***	0.612***	-0.004	0.026	0.041†	0.002
Zinc	-0.02	0.178***	-0.220***	0.129***	-0.013	0.124***	0.623***	-0.037	0.014	-0.012	0.003
Copper	-0.036	0.112***	-0.134***	0.155***	-0.030	0.105***	0.562***	-0.001	-0.01	0.046*	-0.014
Sodium	-0.054*	0.131***	-0.231***	0.083***	0.007	0.054*	0.694***	-0.019	0.041†	-0.021	0.003
Potassium	-0.001	0.213***	0.208***	0.173***	-0.029	0.142***	0.726***	-0.026	-0.005	0.037	0.018
Selenium	-0.065**	0.081***	-0.238***	0.088***	-0.010	0.094***	0.696***	0.011	0.062**	-0.027	0.003
Caffeine	-0.081***	0.139***	-0.087***	0.018	0.040†	0.041†	0.163***	-0.005	-0.024	-0.065**	0.057*
Theobromine	0.034	0.155***	0.006	0.082***	-0.014	0.089***	0.207***	-0.001	0.063**	-0.020	0.003
Alcohol	0.01	0.124***	-0.147***	0.121***	-0.048*	0.107***	0.197***	-0.001	-0.018	-0.072**	-0.023
Meat	0.004	-0.004	-0.088***	-0.020	0.008	-0.004	0.079**	-0.003	0.010	-0.047*	-0.006
Vegetables	0.017	0.127***	-0.015	0.079***	-0.037	0.053*	0.173***	-0.001	0.024	0.046*	0.031
Coffee	-0.206***	0.083***	-0.032	-0.004	0.078**	0.031	0.192***	0.014	-0.021	0.080***	0.038†

***p<.001, **p<.001, *p<.05, †p<.10

Table 7: Pearson Correlation Coefficients among Demographic Variables and Fatty Acids

	Age	Ethnicity	Female	Education	BMI	Physical Activity	Calories	Supplements Use	Antacid Use	Special Diet	Medication Use
SFA4	-0.001	0.212***	-0.060**	0.090***	-0.030	0.033	0.0420***	-0.003	0.020	-0.045*	-0.028
SFA6	-0.003	0.194***	-0.067**	0.068**	-0.033	0.024	0.407***	-0.005	0.009	-0.052*	-0.023
SFA8	-0.002	0.147***	-0.064**	0.050*	-0.036	0.016	0.383***	-0.017	-0.013	-0.051*	-0.013
SFA10	-0.001	0.203***	-0.074**	0.080***	-0.033	0.028	0.445***	-0.010	-0.002	-0.051*	-0.008
SFA12	0.001	0.122***	-0.051*	0.047*	-0.026	0.013	0.346***	-0.019	-0.015	-0.028	0.004
SFA14	-0.024	0.202***	-0.121***	0.078**	-0.020	0.030	0.531***	-0.008	0.012	-0.060**	-0.017
SFA16	-0.003	0.194***	-0.067**	0.068**	-0.033	0.024	0.407***	-0.012	0.036	-0.072**	0.016
SFA18	-0.002	0.147***	-0.064**	0.050*	-0.036	0.016	0.383***	-0.018	0.035	-0.072**	0.016
MFA16_1	-0.124***	0.060**	-0.231***	0.030	0.041†	0.037†	0.572***	-0.005	0.010	-0.038†	0.009
MFA18_1	-0.064**	0.157***	-0.250***	0.067**	0.004	0.072**	0.793***	-0.011	0.031	-0.062**	0.038†
MFA20_1	-0.050*	0.063**	-0.167***	0.058*	-0.007	0.024	0.490***	0.019	0.018	-0.040†	0.028
MFA22_1	0.018	0.039†	-0.065**	0.045*	-0.045*	-0.003	0.105***	0.023	0.044*	-0.030	-0.002
PFA18_2	-0.036	0.120***	-0.142***	0.043†	-0.007	0.078**	0.689***	-0.014	0.026	-0.018	0.036
PFA18_3	-0.027	0.118***	-0.101***	0.036	-0.010	0.078**	0.596***	-0.002	0.003	-0.016	0.001
PFA18_4	-0.009	0.032	-0.038†	0.047*	-0.081***	0.021	0.135***	0.021	0.013	-0.026	0.010
PFA20_4	-0.128***	-0.079**	-0.179***	-0.015	0.065**	0.020	0.319***	-0.014	0.022	-0.034	0.031
PFA20_5	0.016	0.015	-0.014	0.030	-0.041†	0.019	0.102***	0.007	0.009	-0.020	-0.015
PFA22_5	-0.052*	-0.062**	-0.055*	0.038†	-0.013	0.030	0.167***	0.031	-0.003	-0.020	-0.004
PFA22_6	-0.019	-0.023	-0.041†	0.031	-0.037	0.024	0.137***	0.014	0.013	-0.020	-0.013

***p<.001, **p<.001, *p<.05, †p<.10

Table 8: Pearson Correlation Coefficients among Dietary Variables and Depression

	Depression
Protein	-0.092***
Carbohydrates	-0.052*
Sugars	-0.029
Fiber	-0.097***
Total Fat	-0.070**
Cholesterol	-0.039†
Vitamin E	-0.105***
Vitamin A	-0.076**
Alpha Carotene	-0.042†
Beta Carotene	-0.082***
Beta Crypto Xanthin	-0.072**
Lycopene	-0.034
Lutein	-0.125***
Thiamin	-0.089***
Riboflavin	-0.063**
Niacin	-0.105***
Vitamin B6	-0.108***
Folate	-0.101***
Folic Acid	-0.077**
Retinol	-0.058*
Choline	-0.082***
Vitamin B12	-0.070**
Vitamin C	-0.094***
Vitamin K	-0.113***
Calcium	0.060**
Phosphorus	-0.073**
Magnesium	-0.097***
Iron	-0.124***
Zinc	-0.083***
Copper	-0.079***
Sodium	-0.095***
Potassium	-0.104***
Selenium	-0.100***
Caffeine	-0.037
Theobromine	-0.004
Alcohol	-0.084***
Meat	-0.018
Vegetables	-0.105***
Coffee	-0.033

***p<.001, **p<.001, *p<.05, †p<.10

Table 9: Pearson Correlation Coefficients among Fatty Acids and Bowel Measures with Depression

	Depression
SFA4	-0.025
SFA6	-0.019
SFA8	-0.011
SFA10	-0.022
SFA12	-0.006
SFA14	-0.028
SFA16	-0.019
SFA18	-0.011
MFA16_1	-0.046*
MFA18_1	-0.059*
MFA20_1	-0.023
MFA22_1	-0.059**
PFA18_2	-0.083***
PFA18_3	-0.088***
PFA18_4	-0.020
PFA20_4	-0.050*
PFA20_5	-0.073**
PFA22_5	-0.075**
PFA22_6	-0.083***
Bowel	0.124***

***p<.001, **p<.001, *p<.05, †p<.10

Table 10: Factor Component Analysis for the Depression as the Outcome Analysis

	Component										
	1	2	3	4	5	6	7	8	9	10	11
Protein	.163	.541	.280	.262	**.629**	.078	.117	.034	.035	.105	-.041
Carbohydrates	.201	.502	.386	.329	-.032	-.004	.001	.043	**.481**	-.010	.218
Sugars	.222	.344	.192	.150	-.040	-.025	.002	.121	**.627**	.006	.374
Fiber	.044	**.708**	.228	.220	-.114	.360	-.032	-.046	.208	.031	-.021
Total Fat	.385	.197	.166	**.763**	.367	.017	.010	.024	.052	.102	.094
Cholesterol	.210	.021	.008	.254	**.836**	.040	.082	.173	.054	-.034	.023
Vitamin E	.026	.373	.246	**.561**	.096	.386	.107	.084	.044	-.003	.091
Retinol	.354	.152	.340	.050	.177	.127	.028	**.699**	.045	-.130	.098
Vitamin A	.266	.195	.296	.028	.120	.557	.015	**.561**	.043	-.038	.116
Alpha Carotene	-.036	.066	.048	-.033	-.011	**.655**	-.001	.034	.207	.360	.104
Beta Carotene	.028	.157	.067	.041	.011	**.870**	.006	.041	.103	.241	.063
Beta-Crypto	-.055	.114	.038	-.025	.132	.340	.029	.034	**.716**	-.004	-.111
Lycopene	-.006	.148	.048	.057	-.035	.220	.011	-.042	-.006	**.736**	.053
Lutein	.003	.172	.075	.126	.140	**.794**	.035	.061	.128	-.078	-.094
Thiamin	.143	.416	**.738**	.184	.099	.065	.020	.087	.122	.035	-.065
Riboflavin	.286	.452	**.517**	.070	.264	.062	-.006	.433	.066	.018	.035
Niacin	.031	.428	**.649**	.185	.354	.110	.115	-.070	.009	.075	-.013
Vitamin B6	.051	.486	**.572**	.052	.256	.239	.056	.066	.115	.003	.010
Folate	.094	.353	**.757**	.182	.006	.266	.036	.144	.121	-.045	-.026
Folic Acid	.085	-.067	**.894**	.124	-.081	-.005	.008	.095	.044	-.006	.028
Choline	.102	.441	.112	.233	**.729**	.148	.107	.195	.101	-.031	.031
Vitamin B12	.188	.288	**.461**	-.040	.357	-.013	.232	.436	-.060	.127	.065
Vitamin C	-.024	.286	.149	-.021	.032	.488	.072	-.050	**.591**	.046	-.050
Vitamin K	-.006	.208	.095	.367	.006	**.747**	.059	.002	-.048	-.099	-.034
Calcium	.413	**.480**	.266	.101	.046	.067	.049	.468	.174	.054	-.050
Phosphorus	.299	**.670**	.270	.247	.372	.053	.093	.237	.097	.048	.001
Magnesium	.141	**.823**	.256	.238	.105	.223	.068	.064	.143	.013	.055
Iron	.085	.391	**.786**	.159	.117	.108	.016	.114	.063	.063	.050
Zinc	.159	**.544**	.436	.124	.375	.038	-.009	.097	-.006	.258	.027
Copper	.006	**.690**	.188	.221	.125	.192	.089	.098	.010	.063	.138
Sodium	.148	.327	.327	**.460**	.367	.109	.062	-.025	.013	.227	-.091
Potassium	.162	**.729**	.209	.189	.223	.299	.059	.088	.275	.110	.051

Note: Component 12 predictor, alcohol, and Component 13 predictor, caffeine, were intentionally separate from the nutrient predictors presented here

Table 10 Contd.

	Component										
	1	2	3	4	5	6	7	8	9	10	11
Selenium	.124	.401	.310	.296	**.587**	.041	.180	.033	.010	.005	-.057
Theobromine	.111	.089	-.010	.108	-.012	.022	.004	.059	.014	.058	**.848**
SFA4	**.886**	.098	.020	.113	.050	-.010	.007	.267	.043	.092	-.095
SFA6	**.913**	.088	.020	.094	.054	-.008	.012	.236	.039	.026	-.076
SFA8	**.949**	.066	.101	.028	.052	.038	-.013	-.068	-.017	-.075	.125
SFA10	**.973**	.087	.079	.091	.072	.016	-.002	.081	.014	.018	.019
SFA12	**.806**	.041	.137	.032	.065	.067	-.036	-.257	-.019	-.103	.242
SFA14	**.913**	.098	.096	.170	.175	-.048	-.005	.097	.038	.150	.004
SFA16	**.913**	.088	.020	.094	.054	-.008	.012	.236	.039	.026	-.076
SFA18	**.949**	.066	.101	.028	.052	.038	-.013	-.068	-.017	-.075	.125
MFA16_1	.330	.044	.100	.370	**.630**	-.081	.041	-.056	.055	.310	-.085
MFA18_1	.259	.190	.148	**.783**	.361	-.020	-.019	-.010	.045	.123	.095
MFA20_1	.019	.132	.057	**.639**	.225	-.040	.348	-.080	.030	.080	-.047
MFA22_1	-.016	-.079	.088	.175	-.045	-.078	**.576**	.061	.173	.173	-.106
PFA18_2	.022	.202	.149	**.871**	.160	.147	.031	.028	.006	-.066	.079
PFA18_3	.111	.162	.103	**.753**	.107	.235	.054	.114	.014	-.060	.020
PFA18_4	.063	.063	.019	.059	-.021	-.037	**.752**	.020	-.012	.134	.008
PFA20_4	-.068	.008	.007	.156	**.851**	.064	.167	-.003	-.017	-.169	.015
PFA20_5	-.018	.080	.007	.014	.052	.061	**.924**	.042	-.020	-.061	.030
PFA22_5	-.049	.072	.047	.018	.287	.104	**.800**	-.085	-.051	-.121	.045
PFA22_6	-.035	.053	-.008	.041	.191	.089	**.917**	.036	.005	-.128	.020

Note: Component 12 predictor, alcohol, and Component 13 predictor, caffeine, were intentionally separate from the nutrient predictors presented here

Table 11: Factor Analysis for Depression Data Set

Component 1	Component 2	Component 3	Component 4	Component 5	Component 6
SFA4	Fiber	Thiamin	Total Fat	Protein	Alpha Carotene
SFA6	Calcium	Riboflavin	Vitamin E	Cholesterol	Beta Carotene
SFA8	Phosphorus	Niacin	Sodium	Choline	Lutein
SFA10	Magnesium	Vitamin B6	MFA 18_1	Selenium	Vitamin K
SFA12	Zinc	Folate	MFA 20_1	MFA 16_1	
SFA14	Copper	Folic Acid	PFA 18_2	PFA 20_4	
SFA16	Potassium	Vitamin B12	PFA 18_3		
SFA18		Iron			

Component7	Component 8	Component 9	Component 10	Component 11	Component 12
MFA 22_1	Retinol	Carbohydrates	Lycopene	Theobromine	Alcohol
PFA 18_4	Vitamin A	Sugar			
PFA 20_5		Beta-Cryptoxanthin			
PFA 22_5		Vitamin C			
PFA 22_6					

Component 13
Caffeine

Table 12: Moderated Regression with Nutrient Components and Depression with Bowel Function

Predictor	Depression			
	B Coefficient	*SE* B	R^2	ΔR^2
Component 1	1.124	0.924		
Bowel	0.237***	0.071		
Component 1 X Bowel	-0.152	0.363	0.057***	< 0.001
Component 2	-1.494	0.909		
Bowel	0.213***	0.044		
Component 2 X Bowel	-0.484†	0.273	0.060***	0.003†
Component 3	-1.704**	0.628		
Bowel	0.208***	0.043		
Component 3 X Bowel	-0.513*	0.255	0.063***	0.003*
Component 4	-2.036*	1.021		
Bowel	0.219***	0.044		
Component 4 X Bowel	-0.578*	0.259	0.063***	0.004*
Component 5	-1.317*	0.659		
Bowel	0.213***	0.044		
Component 5 X Bowel	-0.505*	0.252	0.061***	0.003*
Component 6	-0.483**	0.182		
Bowel	0.219***	0.044		
Component 6 X Bowel	-0.183*	0.091	0.064***	0.004*
Component 7	-12.222***	3.302		
Bowel	0.211***	0.043		
Component 7 X Bowel	-0.599	1.572	0.061***	< 0.001
Table 12: Contd.	B Coefficient	*SE* B	R^2	ΔR^2
Component 8	-0.281	0.276		
Bowel	0.211***	0.044		
Component 8 X Bowel	0.047	0.107	0.057***	< 0.001
Component 9	-0.557†	0.295		
Bowel	0.209***	0.042		
Component 9 X Bowel	-0.365**	0.141	0.064***	0.006**

Component 10	-0.040	0.054		
Bowel	0.213***	0.043		
Component 10 X Bowel	-0.030	0.027	0.058***	0.001
Component 11	0.163	0.107		
Bowel	0.212***	0.043		
Component 11 X Bowel	0.053	0.049	0.058***	0.001
Component 12	-0.316*	0.151		
Bowel	0.214***	0.043		
Component 12 X Bowel	-0.142*	0.064	0.060***	0.002*
Component 13	-0.085	0.182		
Bowel	0.212***	0.044		
Component 13 X Bowel	-0.010	0.053	0.057***	< 0.001
Meat Consumption	-0.001	0.002		
Bowel	0.213***	0.044		
Meat X Bowel	0.000	0.001	0.056***	< 0.001
Vegetable Consumption	-0.001**	0.001		
Bowel	0.216***	0.044		
Vegetable X Bowel	-0.000*	0.000	0.063***	0.002*

Table 12: Contd.	B Coefficient	*SE* B	R^2	ΔR^2
Coffee Consumption	0.000	0.000		
Bowel	0.212***	0.044		
Coffee X Bowel	0.000	0.000	0.057***	< 0.001

Note. Race, gender, education, being physically active, calories, and physical function are controlled for in the above regressions; Component 1 = short-chain fatty acids; Component 2 = Fiber, Calcium, Phosphorus, Magnesium, Zinc, Copper, and Potassium; Component 3 = Thiamin, Riboflavin, Niacin, Vit B6, Folate, Folic Acid, Vitamin B12, and Iron; Component 4 = Fat, Vit E, Sodium, MFA18_1, MFA20_1, PFA18_2, and PFA18_3; Component 5 = Protein, Cholesterol, Choline, Selenium, MFA 16_1, and PFA20_4 Component 6 = Alpha Carotene, Beta Carotene, Lutein, and Vit K; Component 7 = MFA 22_1, PFA18_4, PFA20_5, PFA22_5 and PFA22_6; Component 8 = Retinol and Vitamin A; Component 9 = Carbohydrates, Sugar, Beta-Crypto-xanthin, and Vitamin C; Component 10 = Lycopene; Component 11 = Theobromine; Component 12 = Alcohol; and Component 13 = Caffeine

****p<.001, **p<.001, *p<.05, †p<.10*

Table 13: Nutrient Composites and the Moderator Value(s) Defining Johnson-Neyman significance region(s)

Predictor	Bowel	Effect	% below	% above
Component 2*	3.271 +	-1.606	63.491	36.509
Component 3*	2.125 +	-1.234	55.922	44.078
Component 4*	2.657 +	-1.815	55.922	44.078
Component 5*	3.188 +	-1.391	63.491	36.509
Component 6*	2.255 +	0.339	55.922	44.078
Component 9**	3.056 +	-0.562	63.491	36.509
Component 12*	3.212 +	-0.340	63.491	36.509
Vegetables*	1.783 +	-0.203	42.989	57.010

Note. Significant indicators are indicative of a significant R^2 increase due to an interaction; (+) is indicative of the reported bowel value and greater; bowel range is from 0 to 20.

***p<.001, **p<.001, *p<.05, †p<.10

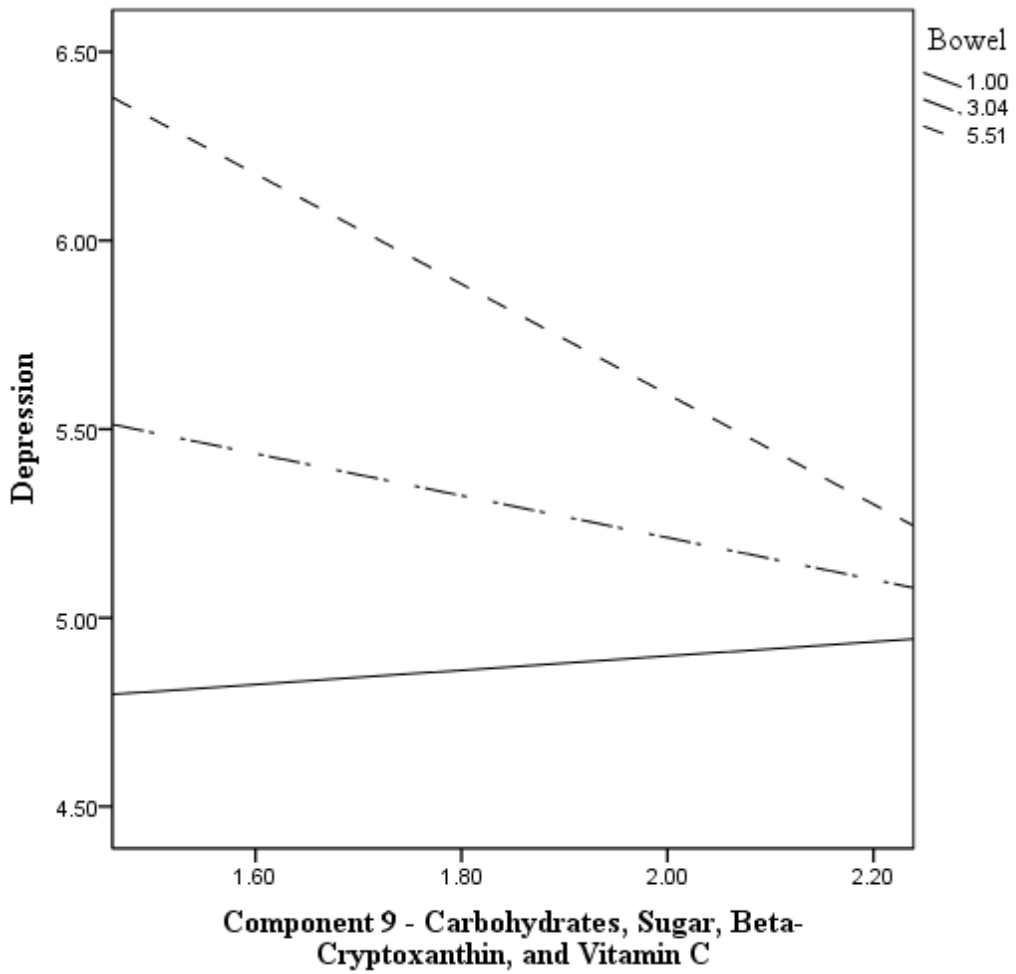

Figure 6: The Moderating Effect of Bowel among Component 9 and Depression

Note. Bowel is representative of the fecal incontinence score (M = 3.04, SD = 2.47). The range of the fecal incontinence measure was on a continuous scale from 1-20.

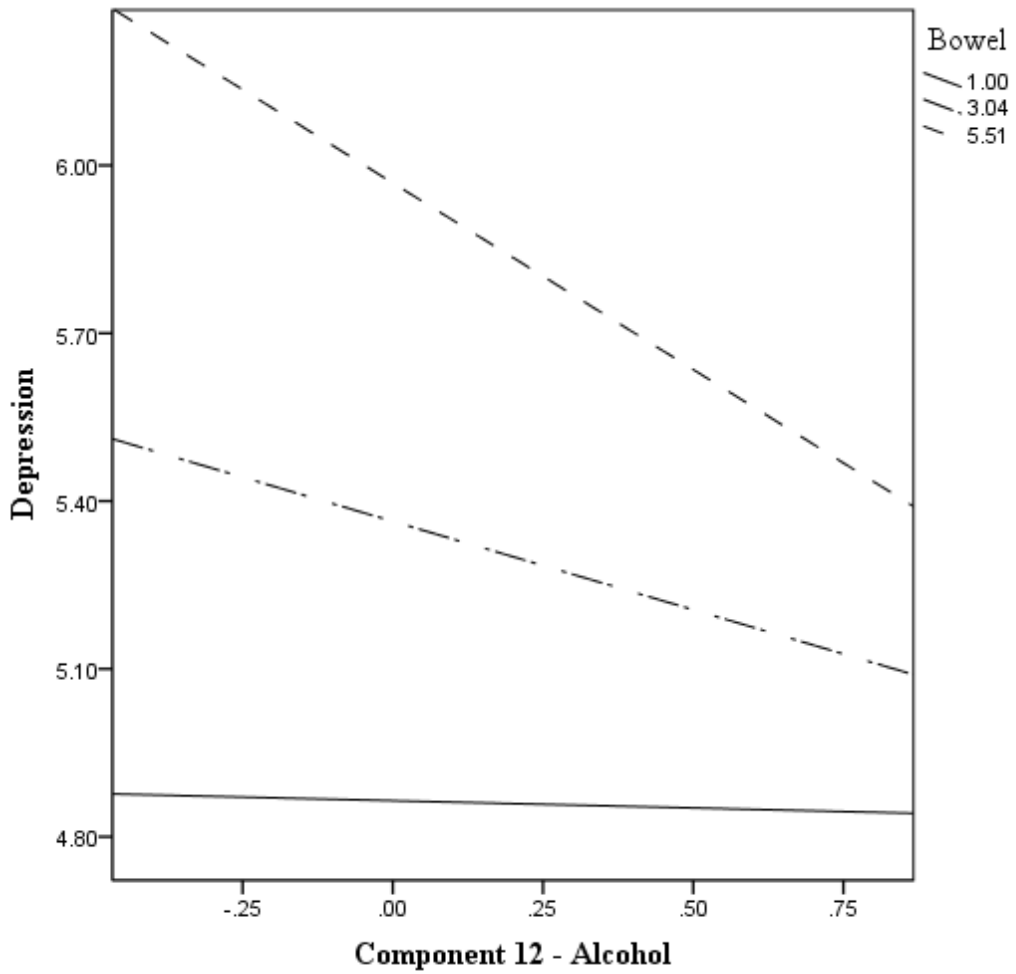

Figure 7: The Moderating Effect of Bowel among Component 12 and Depression

Note. Bowel is representative of the fecal incontinence score (M = 3.04, SD = 2.47). The range of the fecal incontinence measure was on a continuous scale from 1-20.

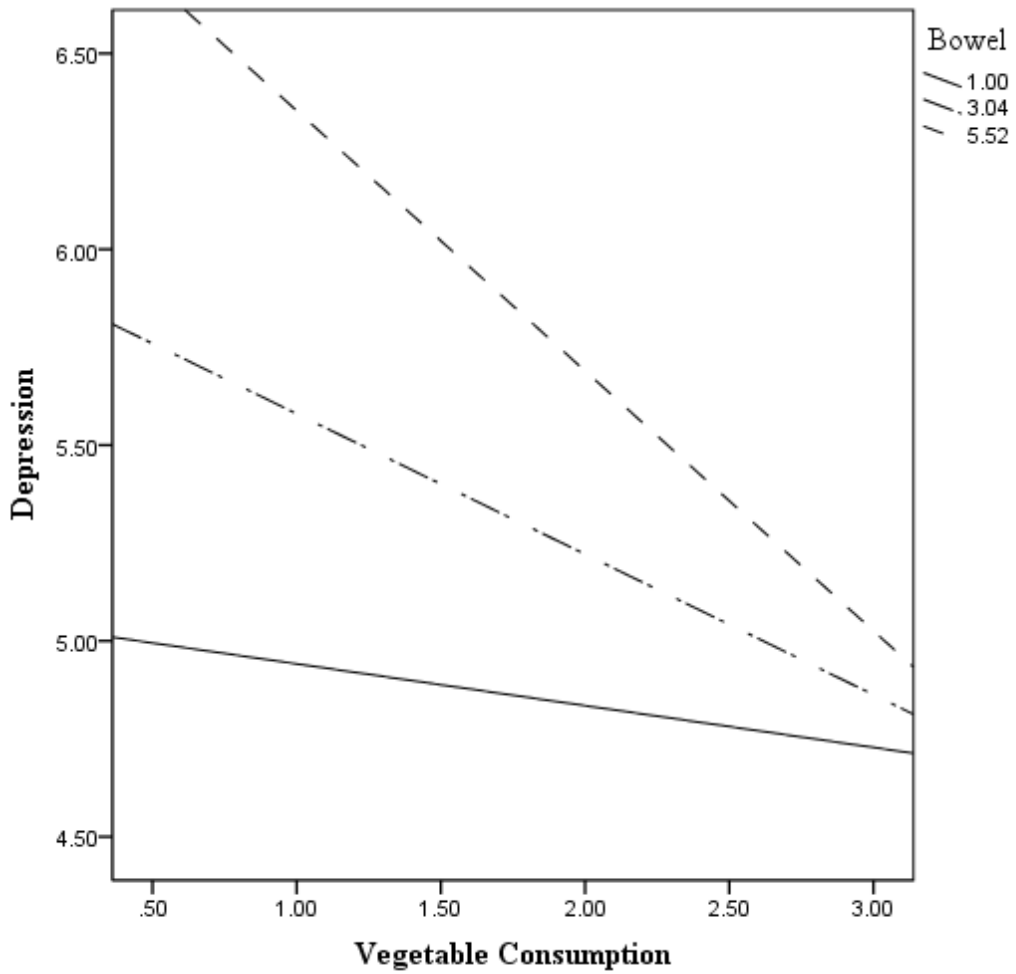

Figure 8: The Moderating effect of Bowel on Vegetable Consumption and Depression

Note. Bowel is representative of the fecal incontinence score (M = 3.04, SD = 2.47). The range of the fecal incontinence measure was on a continuous scale from 1-20.

Table 14: Moderated Regression with Nutrient Components and Depression with Bristol Stool

Predictor	Depression			
	B Coefficient	*SE* B	R^2	ΔR^2
Component 1	2.559	3.218	0.039***	<0.001
Normal	-0.347	0.534		
Diarrhea	-1.249	0.632		
Interaction 1	-1.349	3.289		
Interaction 2	-2.317	3.852		
Component 2	-3.306	2.271	0.041***	0.001
Normal	-4.992	4.348		
Diarrhea	-4.264	5.143		
Interaction 1	2.288	2.182		
Interaction 2	2.138	2.566		
Component 3	-0.834	1.979	0.041***	0.001
Normal	-0.052	2.202		
Diarrhea	1.665	2.663		
Interaction 1	-0.448	2.017		
Interaction 2	-1.662	2.416		
Component 4	1.111	2.252	0.042***	0.002
Normal	2.487	2.541		
Diarrhea	5.512	3.044		
Interaction 1	-2.522	2.162		
Interaction 2	-4.631†	2.527		
Component 5	1.932	2.150	0.041***	0.002
Normal	3.679	2.960		
Diarrhea	6.147†	3.439		
Interaction 1	-3.018	2.161		
Interaction 2	-4.430†	2.466		
Table 14: Contd.	B Coefficient	*SE* B	R^2	ΔR^2
Component 6	-1.894**	0.678	0.046***	0.004†
Normal	-4.139*	1.747		

Diarrhea	-2.861	2.048		
Interaction 1	1.591*	0.699		
Interaction 2	1.233	0.821		
Component 7	-7.327	16.041	0.043***	0.001
Normal	-0.510	0.411		
Diarrhea	0.039	0.458		
Interaction 1	-3.410	16.392		
Interaction 2	-13.664	17.268		
Component 8	-0.146	0.699	0.038***	<0.001
Normal	-0.448	1.885		
Diarrhea	0.808	2.587		
Interaction 1	-0.031	0.729		
Interaction 2	-0.362	0.999		
Component 9	-0.509	1.034	0.039***	<0.001
Normal	-0.431	1.992		
Diarrhea	-0.356	2.233		
Interaction 1	-0.052	1.078		
Interaction 2	0.139	1.198		
Component 10	0.053	0.202	0.038***	<0.001
Normal	-0.339	0.563		
Diarrhea	0.222	0.669		
Interaction 1	-0.082	0.211		
Interaction 2	-0.142	0.244		

Table 14: Contd.	B Coefficient	*SE* B	R^2	ΔR^2
Component 11	-0.703†	0.418	0.042***	0.003†
Normal	-1.249*	0.581		
Diarrhea	-0.865	0.631		
Interaction 1	0.936*	0.430		
Interaction 2	1.030*	0.482		
Component 12	-0.151	0.821	0.041***	0.001
Normal	-0.507	0.370		

Diarrhea	0.060	0.422		
Interaction 1	-0.096	0.831		
Interaction 2	-0.811	0.889		
Component 13	0.106	0.429	0.038***	<0.001
Normal	-0.171	0.710		
Diarrhea	-0.084	0.836		
Interaction 1	-0.219	0.448		
Interaction 2	-0.016	0.511		

Note. Race, gender, education, being physically active, calories, and BMI are controlled for in the above regressions; Component 1 = short-chain fatty acids; Component 2 = Fiber, Calcium, Phosphorus, Magnesium; Zinc; Copper, and Potassium; Component 3 = Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Folic Acid, Vit B12, and Iron; Component 4 = Fat, Vit E, Sodium, MFA18_1, MFA20_1, PFA18_2, and PFA18_3; Component 5 = Protein, Cholesterol, Choline, Selenium, MFA16_1 and PFA 20_4; Component 6 = Alpha Carotene, Beta Carotene, Lutein, and Vit K; Component 7 = MFA22_1, PFA18_4, PFA20_5, PFA22_5, and PFA22_6; Component 8 = Retinol and Vit A; Component 9 = Carbohydrates, Sugar, Beta-Cryto-xanthin, and Vitamin C; Component 10 = Lycopene; Component 11 = Theobromine; Component 12 = Alcohol; Component 13 = Caffeine

****p<.001, **p<.001, *p<.05, †p<.10*

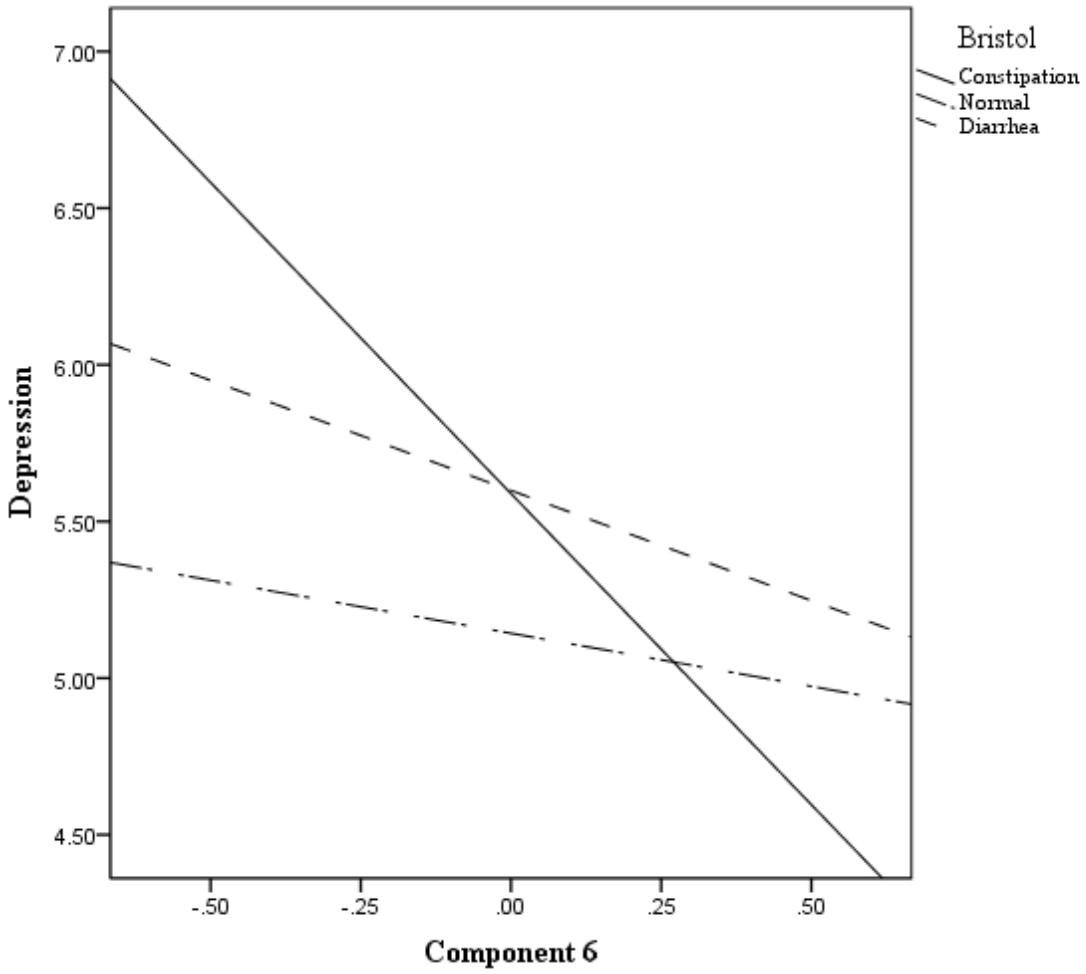

Figure 9: Moderating Effect of the Bristol Stool measure and Component 6 and Depression

Note. Component 6 = alpha carotene, beta carotene, lutein, and vitamin K; The constipation group was the only significant moderator

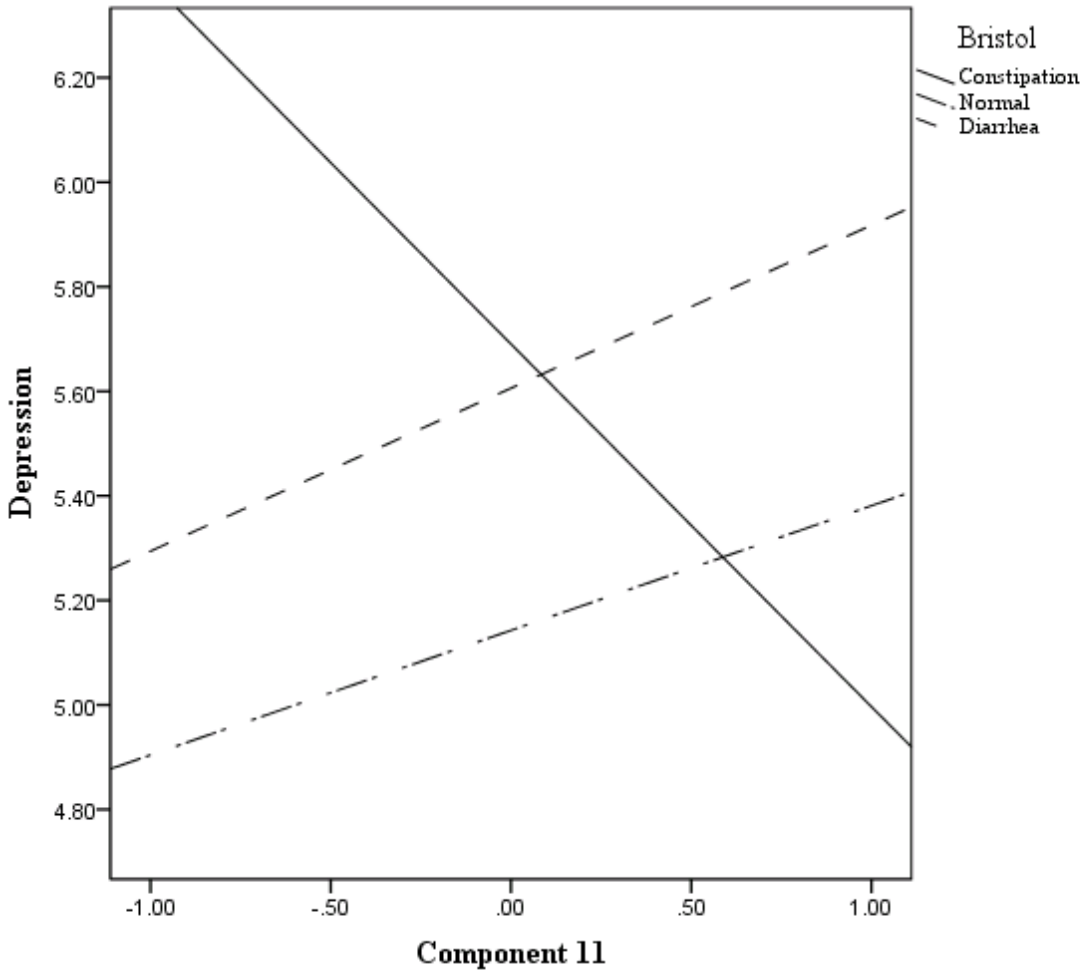

Figure 10: Moderating Effect of Bristol Stool on Component 11 and Depression

Note. Component 11 = theobromine; The constipation and normal group were the only groups to have a near significant effect as a moderator

Table 15: Demographic Characteristics for Physical Function Analytic Sample in the National Health and Nutrition Examination Study

Characteristic	*N* = 1763	
	M (%)	*SD*
Age (y)	73.28	5.38
Physical Function	21.33	2.17
Fecal Incontinence	1.59	2.12
Ethnicity (white)	(64.90)	
Gender (female)	(50.80)	
Education		
less than ninth grade	(15.4)	
9-11 education	(15.9)	
High School graduate/GED	(25.4)	
some college or associates degree	(22.4)	
college graduate or above	(20.9)	
Physically Active	(65.10)	
Overweight	(27.30)	
Bowel Normality	(80.40)	
Constipation	(5.70)	
Diarrhea or Urgency	(13.00)	

Note. Physical function had a possible score of 0-80 in which higher scores were indicative of worse functioning; Fecal incontinence had a possible score of 1-20.

Table 16: Bowel Characteristics for Physical Function Analytic Sample in the NHANES

N = 1763		
Characteristic	*n*	%
Common Stool Type		
Type 1 (separate hard lumps, like nuts)	37	2
Type 2 (sausage-like, but lumpy)	71	3.8
Type 3 (like sausage but with cracks in the surface)	378	20.1
Type 4 (like sausage or snake, smooth and soft)	1133	60.3
Type 5 (soft blobs with clear-cut edges)	115	6.1
Type 6 (fluffy pieces with ragged edges, a mushy stool)	130	6.9
Type 7 (watery, no solid pieces)	16	0.9

Table 17: Dietary Characteristics for Physical Function Analytic Sample in the National Health and Nutrition Examination Study

	N = 1763				
Characteristic	*M*	*SD*		*M*	*SD*
Protein (gm)	66.94	28.280	Energy (kcal)	1674.26	576.32
Total Fat (gm)	63.29	29.590	Meat (gm)	22.71	59.64
Cholesterol (mg)	239.88	190.59	Vegetables (gm)	124.42	151.44
Choline (mg)	287.42	141.54	Coffee (gm)	1585.42	1293.30
Phosphorus (mg)	1119.13	457.26	Sugar (gm)	92.72	50.33
Sodium (mg)	2776.44	1221.16	Potassium (mg)	2427.01	1021.31
Selenium (mcg)	90.74	44.08	Vitamin E (mg)	6.66	4.32
Thiamin (mg)	1.44	0.76	α Carotene (mcg)	455.38	979.92
Niacin (mg)	20.58	9.99	β Carotene (mcg)	2393.56	3689.10
Vitamin B6 (mg)	1.77	1.03	Lutein (mcg)	1591.07	3389.04
Folate (mcg)	194.44	102.96	Vitamin K (mcg)	103.66	164.64
Folic Acid (mcg)	167.58	154.33	Retinol (mcg)	409.47	377.94
Iron (mg)	13.88	7.43	Vitamin A (mcg)	632.52	506.71
Carbohydrates (gm)	206.46	78.74	Riboflavin (mg)	1.95	0.95
Sugars (gm)	91.99	50.89	Vitamin B12 (mcg)	4.80	4.65
Fiber (gm)	15.63	8.23	Calcium (mg)	799.45	450.87
Beta-crytoxanthin	112.50	263.01	Alcohol (gm)	5.78	14.40
Vitamin C (mg)	84.54	77.43	Lycopene (mcg)	4489.77	7996.64
Magnesium (mg)	261.80	110.06	Caffeine (mg)	151.68	172.64
Copper (mg)	1.17	0.67	Zinc (mg)	10.38	6.05
Theobromine (mg)	29.74	59.36			

Table 18: Fatty Acid Characteristics for Physical Function Analytic Sample in the National Health and Nutrition Examination Study

Characteristics	*M* (%)	*SD*
Saturated Fatty Acids (gm)	20.48	11.09
SFA 4:0 (Butanoic) (gm)	0.42	0.43
SFA 6:0 (Hexanoic)	0.24	0.24
SFA 8:0 (Octanoic)	0.19	0.22
SFA 10:0 (Decanoic)	0.35	0.34
SFA 12:0 (Dodecanoic)	0.61	1.01
SFA 14:0 (Tetradecanoic)	1.66	1.34
SFA 16:0 (Hexadecanoic)	11.11	5.63
SFA 18:0 (Octadecanoic)	5.27	2.89
Monounsaturated Fatty Acids (gm)	23.15	11.74
MFA 16:1 (Hexadecenoic)	0.94	0.64
MFA 18:1 (Octadecenoic)	21.7	11.07
MFA 20:1 (Eicosenoic)	0.21	0.23
MFA 22:1 (Docosenoic)	0.03	0.20
Polyunsaturated Fatty Acids (gm)	14.06	7.85
PFA 18:2 (Octadecadienoic)	12.35	7.03
PFA 18:3 (Octadecatrienoic)	1.3	0.95
PFA 18:4 (Octadecatetraenoic)	0.01	0.03
PFA 20:4 (Eicosatentaenoic)	0.12	0.12
PFA 20:5 (Eicosapentaenoic)	0.04	0.13
PFA 22:5 (Docosapentaenoic)	0.02	0.04
PFA 22:6 (Docosahexaenoic)	0.08	0.19

Table 19. Pearson Correlation Coefficients among Demographic Variables and Physical Function

	Physical Function	Bowel
Age	0.090***	-0.020
Ethnicity	-0.029	-0.045†
Female	0.145***	0.030
Education	-0.092***	0.061*
BMI	0.190***	-0.001
Physical Activity	-0.189***	0.040†
Calories	-0.091***	0.092***
Supplement Use	0.011	0.072**
Antacid Use	0.018	0.020
Prescription Data Use	-0.026	-0.002
Special Diet	0.030	0.049*
Depression	0.224***	0.144***

***p<.001, **p<.001, *p<.05, †p<.10

Note. The physical function is scored so that higher numbers are representative of worse function

Table 20. Pearson Correlation Coefficients among Demographic Variables and Dietary Measures

	Age	Ethnicity	Female	Education	BMI	Physical Activity	Calories	Suppl Use	Antacid Use	Rx Use	Special Diet	Depression
Protein	-0.151***	0.077**	-0.256***	0.115***	-0.013	0.090***	0.723***	-0.012	-0.020	-0.019	0.002	-0.037
Carbohydrates	-0.061**	0.086***	-0.186***	0.130***	-0.088***	0.087***	0.817***	0.002	-0.026	-0.021	0.021	0.009
Sugars	-0.015	0.088***	-0.111***	0.112***	-0.083***	0.073**	0.603***	-0.005	-0.016	-0.015	0.016	0.005
Fiber	-0.057*	0.086***	-0.098***	0.222***	-0.075**	0.165***	0.484***	-0.001	0.006	0.008	0.106***	-0.007
Total Fat	-0.111***	0.160***	-0.212***	0.088***	0.000	0.014	0.833***	0.009	-0.063**	-0.025	-0.058*	0.005
Cholesterol	-0.090***	0.017	-0.193***	-0.015	0.022	-0.034	0.421***	0.010	-0.011	-0.002	-0.053*	-0.018
Vitamin E	-0.054*	0.161***	-0.082***	0.179***	-0.071**	0.116***	0.492***	0.004	-0.013	-0.011	0.017	-0.003
Retinol	0.053*	0.146***	-0.052*	0.032	-0.062**	0.010	0.306***	0.021	-0.019	-0.025	0.030	-0.039
Vitamin A	0.024	0.106***	-0.053*	0.059*	-0.096***	0.079**	0.293***	0.000	-0.016	-0.006	0.054*	-0.045†
Alpha Carotene	-0.022	0.022	-0.001	0.032	-0.063**	0.068**	0.067**	-0.010	0.025	0.010	0.046†	0.000
Beta Carotene	-0.025	-0.008	-0.021	0.053*	-0.072**	0.106***	0.096***	-0.036	0.013	-0.002	0.030	-0.028
Beta Cryptoxanthin	0.048*	-0.002	-0.049*	0.033	-0.046*	0.055*	0.073**	-0.004	0.020	-0.002	0.034	0.033
Lycopene	-0.063**	0.083***	-0.031	0.086***	-0.001	0.066**	0.155***	0.015	0.048*	-0.028	-0.004	-0.008
Lutein	-0.001	-0.062**	-0.022	0.033	-0.043†	0.045†	0.048*	-0.014	0.021	-0.015	0.033	-0.045†
Thiamin	-0.029	0.147***	-0.158***	0.101***	-0.070**	0.088***	0.526***	-0.016	-0.014	-0.025	0.037	-0.008
Riboflavin	-0.037	0.255***	-0.167***	0.091***	-0.060**	0.109***	0.575***	0.005	-0.018	-0.015	0.054*	-0.019
Niacin	-0.097	0.142***	-0.220***	0.132***	-0.062**	0.143***	0.605***	-0.033	-0.003	-0.022	0.019	-0.048*
Vitamin B6	-0.048*	0.152***	-0.159***	0.135***	-0.070**	0.153***	0.490***	-0.032	0.022	-0.027	0.059*	-0.033
Folate	-0.033	0.141***	-0.131***	0.150***	0.093***	0.134***	0.478***	-0.015	0.002	-0.026	0.047*	-0.031
Folic Acid	0.023	0.149***	-0.070**	0.057*	-0.055*	0.078**	0.296***	-0.027	0.013	-0.027	0.010	-0.012
Choline	-0.107***	0.086***	-0.266***	0.061**	-0.025	0.057*	0.623***	-0.007	-0.010	-0.019	-0.015	-0.030
Vitamin B12	-0.027	0.132***	-0.107***	0.071**	-0.056*	0.016	0.311***	-0.017	0.019	-0.044†	0.012	-0.029
Vitamin C	-0.001	0.030	-0.057*	0.162***	-0.050*	0.116***	0.250***	-0.044†	0.030	0.008	0.083***	-0.031
Vitamin K	-0.034	-0.062**	-0.031	0.035	-0.032	0.047*	0.107***	-0.026	0.000	0.002	0.043†	-0.050*
Calcium	-0.058*	0.158***	-0.072**	0.109***	-0.055*	0.089***	0.497***	-0.002	-0.034	-0.017	0.060*	0.006
Phosphorus	-0.110***	0.170***	-0.224***	0.139***	-0.046*	0.113***	0.760***	-0.005	-0.036	-0.016	0.037	-0.013
Magnesium	-0.098***	0.130***	-0.174***	0.230***	-0.082***	0.190***	0.668***	0.006	-0.016	-0.005	0.078**	-0.018
Iron	-0.034	0.140***	-0.164***	0.107***	-0.071**	0.116***	0.536***	-0.020	-0.002	-0.029	0.056*	-0.031
Zinc	-0.073**	0.164***	-0.181***	0.101***	-0.016	0.094***	0.541***	-0.022	-0.034	0.005	0.037	-0.012
Copper	-0.061**	0.075**	-0.115***	0.165***	-0.053*	0.085***	0.476***	0.001	-0.013	0.001	0.061*	-0.036
Sodium	-0.126***	0.112***	-0.222***	0.073**	0.008	0.028	0.652***	0.003	-0.010	-0.012	-0.038	0.001
Potassium	-0.074**	0.202***	-0.198***	0.190***	-0.071**	0.172***	0.687***	-0.015	0.009	-0.006	0.066**	-0.033
Selenium	-0.132***	0.047*	-0.215***	0.096***	-0.041†	0.069**	0.641***	0.001	-0.005	-0.019	-0.026	-0.049*
Caffeine	-0.072**	0.208***	-0.092***	-0.012	0.008	0.027	0.163***	0.004	0.004	0.010	-0.036	-0.022
Theobromine	-0.010	0.077**	-0.017	0.059*	-0.006	0.034	0.220***	0.007	-0.033	0.007	-0.029	0.027
Alcohol	-0.034	0.091***	-0.175***	0.101***	-0.081***	0.082***	0.226***	0.007	0.032	-0.007	-0.086***	-0.045†
Meat	-0.010	-0.012	-0.120***	-0.038†	0.012	-0.008	0.130***	-0.016	0.009	0.035	-0.038	-0.023
Vegetables	-0.010	0.141***	-0.082***	0.095***	-0.059*	0.107***	0.187***	-0.026	-0.009	0.006	0.053*	-0.044†
Coffee	-0.226***	0.069**	-0.091***	0.031	0.081***	0.099***	0.222***	0.003	-0.013	0.006	0.044†	-0.034

***$p < .001$, **$p < .001$, *$p < .05$, †$p < .10$

Table 21. Pearson Correlation Coefficients among Demographic Variables and Fatty Acids

	Age	Ethnicity	Female	Education	BMI	Physical Activity	Calories	Suppl Use	Antacid Use	Rx Use	Special Diet	Depression
SFA4	-0.009	0.207***	-0.031	0.033	-0.034	0.011	0.413***	-0.002	-0.043†	0.012	-0.039	0.000
SFA6	-0.002	0.186***	-0.046*	0.024	-0.038†	0.009	0.411***	0.000	-0.043†	0.004	-0.047*	-0.001
SFA8	0.002	0.119***	-0.040†	0.016	-0.046*	-0.014	0.367***	0.007	-0.046†	0.005	-0.038	0.000
SFA10	-0.008	0.191***	-0.035	0.028	-0.037	0.007	0.432***	0.000	-0.038	0.005	-0.045†	-0.001
SFA12	0.000	0.061**	-0.014	0.013	-0.030	-0.023	0.255***	-0.013	-0.042†	0.012	-0.029	-0.010
SFA14	-0.039†	0.184***	-0.082***	0.03	-0.015	-0.016	0.514***	0.000	-0.042†	-0.001	-0.046†	-0.001
SFA16	-0.102***	0.163***	-0.202***	0.024	0.009	-0.020	0.771***	0.013	-0.059*	-0.015	-0.061*	0.010
SFA18	-0.079**	0.168***	-0.197***	0.016	0.007	-0.015	0.732***	-0.002	-0.054*	-0.022	-0.070**	0.014
MFA16_1	-0.143***	0.046*	-0.225***	0.037†	0.076**	-0.041†	0.560***	0.017	-0.023	-0.011	-0.045†	-0.009
MFA18_1	-0.107***	0.133***	-0.234***	0.072**	-0.005	0.028	0.782***	0.009	-0.043*	-0.019	-0.065**	0.005
MFA20_1	-0.082***	0.028	-0.139***	0.024	-0.018	0.001	0.395***	0.027	-0.056*	-0.018	-0.043†	-0.027
MFA22_1	0.016	0.018	-0.064**	-0.003	-0.022	-0.026	0.071**	0.022	0.028	-0.033	0.002	-0.040†
PFA18_2	-0.090***	0.105***	-0.117***	0.078**	-0.001	-0.039†	0.651***	0.008	-0.063**	0.043†	-0.028	0.015
PFA18_3	0.041†	0.101***	-0.046*	0.078**	-0.032	0.041†	0.466***	0.000	-0.061*	-0.032	-0.011	-0.001
PFA18_4	0.038†	-0.001	-0.033	0.021	-0.072**	0.028	0.117***	0.020	0.033	-0.003	-0.006	-0.030
PFA20_4	-0.120***	-0.083***	-0.170***	0.02	0.048*	-0.016	0.332***	0.010	-0.014	0.005	-0.036	-0.033
PFA20_5	-0.014	0.223***	-0.027	0.019	-0.066**	0.016	0.110***	-0.010	-0.014	0.016	-0.014	-0.037
PFA22_5	-0.078**	0.369***	-0.062**	0.03	-0.025	0.009	0.169***	0.004	0.025	-0.012	-0.015	-0.050*
PFA22_6	-0.046*	0.304***	-0.049*	0.024	-0.060**	0.017	0.149***	0.004	0.012	0.005	-0.008	-0.051*

***p <.001, **p <.001, *p <.05, †p <.10

Table 22. Pearson Correlation Coefficients among Dietary Variables and Physical Function

Nutrients		Physical Function	
Protein	-0.120***	Choline	-0.121***
Carbohydrates	0.083***	Vitamin B12	-0.077**
Sugars	-0.078**	Vitamin C	-0.091***
Fiber	-0.083***	Vitamin K	-0.058*
Total Fat	-0.067**	Calcium	-0.057*
Cholesterol	-0.077**	Phosphorus	-0.105***
Vitamin E	-0.096***	Magnesium	-0.117***
Retinol	-0.028	Iron	-0.076**
Vitamin A	-0.068**	Zinc	-0.071**
Alpha Carotene	-0.033	Copper	0.083***
Beta Carotene	-0.072**	Sodium	-0.041†
Beta Crypto Xanthin	-0.050*	Potassium	-0.122***
Lycopene	-0.050*	Selenium	-0.099***
Lutein	-0.057*	Caffeine	-0.024
Thiamin	-0.071**	Theobromine	-0.012
Riboflavin	-0.089***	Alcohol	-0.084***
Niacin	-0.127***	Meat	-0.022
Vitamin B6	-0.117***	Vegetables	-0.029
Folate	-0.068**	Coffee	-0.044†
Folic Acid	-0.017		

***p <.001, **p <.001, *p <.05, †p <.10

Note. The physical function is scored so that higher numbers are representative of worse physical function

Table 23. Pearson Correlation Coefficients among Fatty Acids and Bowel Measures with Physical Function

	Physical Function
SFA4	-0.002
SFA6	0.000
SFA8	0.017
SFA10	0.000
SFA12	0.018
SFA14	-0.009
SFA16	-0.051*
SFA18	-0.050*
MFA16_1	-0.073**
MFA18_1	-0.074**
MFA20_1	-0.069**
MFA22_1	-0.041†
PFA18_2	-0.048*
PFA18_3	-0.051*
PFA18_4	-0.056*
PFA20_4	-0.082***
PFA20_5	-0.065**
PFA22_5	-0.071**
PFA22_6	-0.073**
Bowel	0.053*

***p <.001, **p <.001, *p <.05, †p <.10

Note. The physical function is scored so that higher numbers are representative of worse physical function

Table 24: Factor Component Analysis for the Physical Function Analytic Sample

	Component									
	1	2	3	4	5	6	7	8	9	10
Protein	.516	.165	**.643**	.213	.088	.146	.320	.032	-.016	.121
Carbohydrates	.550	.179	.023	.285	.121	.002	.173	**.592**	-.027	-.001
Sugars	.303	.194	.022	.105	.168	.009	.060	**.784**	.091	.008
Fiber	.479	.054	-.109	.222	.415	-.019	**.532**	.175	-.113	.032
Total Fat	.244	.387	.409	**.735**	.013	.015	.030	.155	-.013	.076
Cholesterol	.056	.234	**.848**	.198	.019	.079	-.069	.048	.140	-.041
Vitamin E	.396	.051	.069	**.566**	.366	.107	.224	.051	.086	.040
Vitamin A	.389	.282	.087	.058	.526	.034	-.032	.103	**.564**	.015
Alpha Carotene	.073	-.026	-.070	.019	**.651**	-.008	-.012	.100	.071	.425
Beta Carotene	.098	.016	-.018	.094	**.851**	.021	.054	.007	.118	.307
Beta-Cryptoxanthin	.120	-.008	.158	-.123	**.530**	.040	.011	.436	-.239	-.092
Lycopene	.105	.022	-.006	.041	.164	-.014	.060	.044	-.034	**.790**
Lutein	.132	.023	.147	.143	**.814**	.027	.092	-.072	.057	-.101
Thiamin	**.858**	.124	.058	.161	.098	.065	.077	.071	.000	-.004
Riboflavin	**.714**	.307	.250	.080	.067	.007	.157	.146	.320	-.003
Niacin	**.777**	.023	.301	.179	.119	.126	.118	-.008	-.095	.092
Vitamin B6	**.759**	.047	.196	.055	.283	.072	.176	.056	.006	-.019
Folate	**.849**	.088	-.054	.179	.274	.025	.076	.049	.039	-.065
Folic Acid	**.800**	.065	-.155	.104	-.055	-.009	-.354	.034	.088	-.009
Retinol	.438	.384	.150	.047	.068	.025	-.080	.181	**.627**	-.133
Choline	.337	.124	**.756**	.205	.149	.133	.266	.098	.128	-.033
Vitamin B12	**.623**	.209	.293	-.022	-.017	.253	.006	.058	.311	.092
Vitamin C	.285	-.009	.036	-.081	**.649**	.075	.147	.358	-.177	.012
Vitamin K	.145	-.023	.027	.379	**.729**	.051	.135	-.128	.079	-.080
Calcium	**.497**	.415	.114	.046	.129	.045	.296	.211	.343	.075
Phosphorus	**.569**	.301	.421	.213	.072	.131	.412	.166	.166	.066
Magnesium	.559	.145	.131	.245	.274	.096	**.624**	.181	.014	.033
Iron	**.884**	.062	.073	.174	.101	.012	.041	.090	.053	.040

Table 24: Contd.	1	2	3	4	5	6	7	8	9	10
Zinc	**.665**	.152	.395	.118	.049	-.038	.246	.061	-.007	.221
Copper	.450	.045	.109	.295	.217	.093	**.541**	.177	-.006	.083
Sodium	**.451**	.163	.379	.414	.104	.057	.088	.016	-.074	.237
Potassium	**.529**	.171	.248	.172	.374	.097	.495	.251	.002	.117
Selenium	.487	.125	**.573**	.238	.022	.210	.198	-.014	.012	.032
Theobromine	-.046	.083	-.041	.245	-.096	-.029	.143	**.441**	.218	.156
SFA4	.094	**.904**	.106	.045	.004	-.023	.072	.026	.175	.083
SFA6	.086	**.928**	.103	.038	.008	-.016	.069	.028	.158	.028
SFA8	.099	**.948**	.035	.067	.019	-.007	.019	.051	-.022	-.053
SFA10	.115	**.973**	.088	.074	.025	-.017	.036	.036	.055	.018
SFA12	.104	**.806**	.008	.117	.034	-.013	-.034	.072	-.156	-.071
SFA14	.151	**.912**	.212	.141	-.035	-.002	-.006	.082	.020	.120
SFA16	.086	**.928**	.103	.038	.008	-.016	.069	.028	.158	.028
SFA18	.099	**.948**	.035	.067	.019	-.007	.019	.051	-.022	-.053
MFA16_1	.153	.323	**.657**	.320	-.041	.040	-.104	.028	-.189	.185
MFA18_1	.228	.262	.405	**.750**	-.021	-.016	.022	.160	-.045	.083
MFA20_1	.155	.028	.163	**.590**	-.003	.459	.047	.034	-.143	.025
MFA22_1	.059	-.027	-.020	.164	-.017	**.615**	-.121	.101	-.124	.015
PFA18_2	.212	.033	.190	**.865**	.113	.018	.090	.085	.051	-.024
PFA18_3	.162	.092	.148	**.728**	.222	.067	.089	.038	.118	-.034
PFA18_4	.050	.019	.002	.028	-.009	**.816**	.022	.008	.025	.060
PFA20_4	.027	-.036	**.819**	.143	.064	.170	-.032	-.087	.034	-.148
PFA20_5	.060	-.017	.039	.005	.037	**.940**	.071	-.012	.063	-.017
PFA22_5	.062	-.050	.265	-.010	.091	**.764**	.071	-.066	.024	-.029
PFA22_6	.045	-.029	.165	.015	.066	**.921**	.079	-.038	.085	-.069

Table 25: Factor Analysis Physical Function Data Set

Component 1	Component 2	Component 3	Component 4	Component 5	Component 6
Thiamin	SFA4	Protein	Total Fat	Alpha Carotene	MFA22_1
Riboflavin	SFA6	Cholesterol	Vitamin E	Beta Carotene	PFA18_4
Niacin	SFA8	Choline	MFA18_1	Beta-Cryptoxanthin	PFA20_5
Vitamin B6	SFA10	Selenium	MFA20_1	Lutein	PFA22_5
Folate	SFA12	MFA16_1	PFA18_1	Vitamin C	PFA22_6
Folic Acid	SFA14	PFA20_4	PFA18_3	Vitamin K	
Vitamin B12	SFA16				
Calcium	SFA18				
Phosphorus					
Potassium					
Iron					
Sodium					
Zinc					

Component 7	Component 8	Component 9	Component 10	Component 11	Component 12
Fiber	Carbohydrates	Vitamin A	Lycopene	Alcohol	Caffeine
Magnesium	Sugar	Retinol			
Copper	Theobromine				

Table 26: Moderated Regression with Nutrient Components and Physical Function with Bowel Function

Predictor	Physical Function			
	B Coefficient	*SE* B	R^2	ΔR^2
Component 1	-0.156	0.469		
Bowel	0.059*	0.26		
Component 1 X Bowel	0.061	0.175	0.123***	< 0.001
Component 2	0.266	0.559		
Bowel	0.059*	0.026		
Component 2 X Bowel	0.016	0.246	0.123***	< 0.001
Component 3	-0.553	0.424		
Bowel	0.060*	0.027		
Component 3 X Bowel	-0.083	0.163	0.124***	< 0.001
Component 4	-0.192	0.504		
Bowel	0.061*	0.027		
Component 4 X Bowel	-0.027	0.504	0.123***	< 0.001
Component 5	-0.249	0.117		
Bowel	0.062*	0.027		
Component 5 X Bowel	0.001	0.067	0.125***	< 0.001
Component 6	-2.886**	1.359		
Bowel	0.059*	0.026		
Component 6 X Bowel	-0.611	0.749	0.125***	< 0.001

Table 26: Contd.

Component 7	-0.518	0.442		
Bowel	0.061*	0.027		
Component 7 X Bowel	-0.119	0.186	0.124***	< 0.001
Component 8	0.158	0.161		
Bowel	0.061*	0.026		
Component 8 X Bowel	0.038	0.077	0.124***	< 0.001
Component 9	-0.153	0.191		
Bowel	0.060*	0.027		
Component 9 X Bowel	0.018	0.109	0.123***	< 0.001
Component 10	-0.057†	0.032		
Bowel	0.060*	0.026		
Component 10 X Bowel	-0.012	0.017	0.125***	< 0.001
Component 11	-0.056	0.074		
Bowel	0.059*	0.026		
Component 11 X Bowel	-0.052	0.034	0.124***	< 0.001
Component 12	-0.054	0.064		
Bowel	0.061*	0.026		
Component 12 X Bowel	0.013	0.034	0.123***	< 0.001
Meat Consumption	0.000	0.001		
Bowel	0.060*	0.026		
Meat X Bowel	0.000	0.001	0.123***	< 0.001

Table 26: Contd.

Vegetable Consumption	0.000	0.000		
Bowel	0.057*	0.026		
Vegetable X Bowel	0.000	0.000	0.124***	0.001
Coffee Consumption	0.000†	0.000		
Bowel	0.060*	0.026		
Coffee X Bowel	0.000	0.000	0.126***	0.001

Note. Race, gender, education, being physically active, calories, BMI, supplement use, antacid use, special diet, prescription drug use, and depression are controlled for

****p<.001, **p<.001, *p<.05, †p<.10*

Table 27: Moderated Regression with Nutrient Components and Physical Function with Bristol Stool

Predictor	Physical Function			
	B Coefficient	*SE* B	R^2	ΔR^2
Component 1	2.346	1.479	0.123***	0.002
Normal	-0.419	0.284		
Diarrhea	-0.287	0.313		
Interaction 1	-2.611†	1.452		
Interaction 2	-2.381	1.697		
Component 2	-1.332	1.901	0.122***	0.001
Normal	-0.321	0.271		
Diarrhea	-0.175	1.955		
Interaction 1	1.729	1.955		
Interaction 2	2.502	2.541		
Component 3	-0.093	1.378	0.125***	0.003
Normal	-0.331	0.287		
Diarrhea	-0.172	0.318		
Interaction 1	-0.729	1.389		
Interaction 2	1.211	1.613		
Component 4	0.389	1.352	0.124***	0.002
Normal	-0.335	0.281		
Diarrhea	-0.182	0.313		
Interaction 1	-0.852	1.338		
Interaction 2	1.007	1.566		
Component 5	-0.118	0.478	0.124***	0.001
Normal	-0.324	0.271		
Diarrhea	-0.205	0.301		
Interaction 1	-0.075	0.489		
Interaction 2	-0.431	0.581		
Component 6	-13.103*	6.241	0.125***	0.003**
Normal	-0.331	0.277		
Diarrhea	-0.225	0.298		
Interaction 1	12.015†	6.391		
Interaction 2	2.998	6.941		

Table 27: Contd.	B Coefficient	*SE* B	R^2	ΔR^2

Component 7	-1.378	1.321	0.122***	0.000
Normal	-0.301	0.268		
Diarrhea	-0.166	0.300		
Interaction 1	0.914	1.341		
Interaction 2	1.112	1.611		
Component 8	-0.017	0.701	0.122***	0.000
Normal	-0.318	0.270		
Diarrhea	-0.176	0.302		
Interaction 1	0.149	0.708		
Interaction 2	0.379	0.829		
Component 9	1.242†	0.660	0.125***	0.004†
Normal	-0.326	0.267		
Diarrhea	-0.197	0.298		
Interaction 1	-1.499*	0.678		
Interaction 2	-1.293	0.794		
Component 10	-0.024	0.154	0.123***	0.000
Normal	-0.310	0.279		
Diarrhea	-0.184	0.311		
Interaction 1	-0.036	0.158		
Interaction 2	-0.014	0.178		
Component 11	-0.396	0.451	0.122***	0.000
Normal	-0.288	0.265		
Diarrhea	-0.155	0.297		
Interaction 1	0.358	0.456		
Interaction 2	0.292	0.494		
Component 12	-0.321	0.358	0.122***	0.001
Normal	-0.302	0.271		
Diarrhea	-0.173	0.303		
Interaction 1	0.300	0.364		
Interaction 2	0.186	0.406		

Table 27: Contd.	B Coefficient	SE B	R^2	ΔR^2

Meat Consumption	0.008	0.008	0.122***	0.001
Normal	-0.383	0.286		
Diarrhea	-0.251	0.317		
Interaction 1	-0.008	0.008		
Interaction 2	-0.009	0.009		
Vegetable Consumption	0.000	0.001	0.122***	0.000
Normal	-0.321	0.269		
Diarrhea	-0.199	0.302		
Interaction 1	0.000	0.001		
Interaction 2	0.001	0.002		
Coffee Consumption	0.000	0.000	0.123***	0.000
Normal	-0.321	0.283		
Diarrhea	-0.202	0.315		
Interaction 1	0.000	0.000		
Interaction 2	0.000	0.000		

Note. Race, gender, education, being physically active, calories, BMI, supplement use, antacid use, prescription drug use, on a special diet, and depression are controlled for

****p<.001, **p<.001, *p<.05, †p<.10*

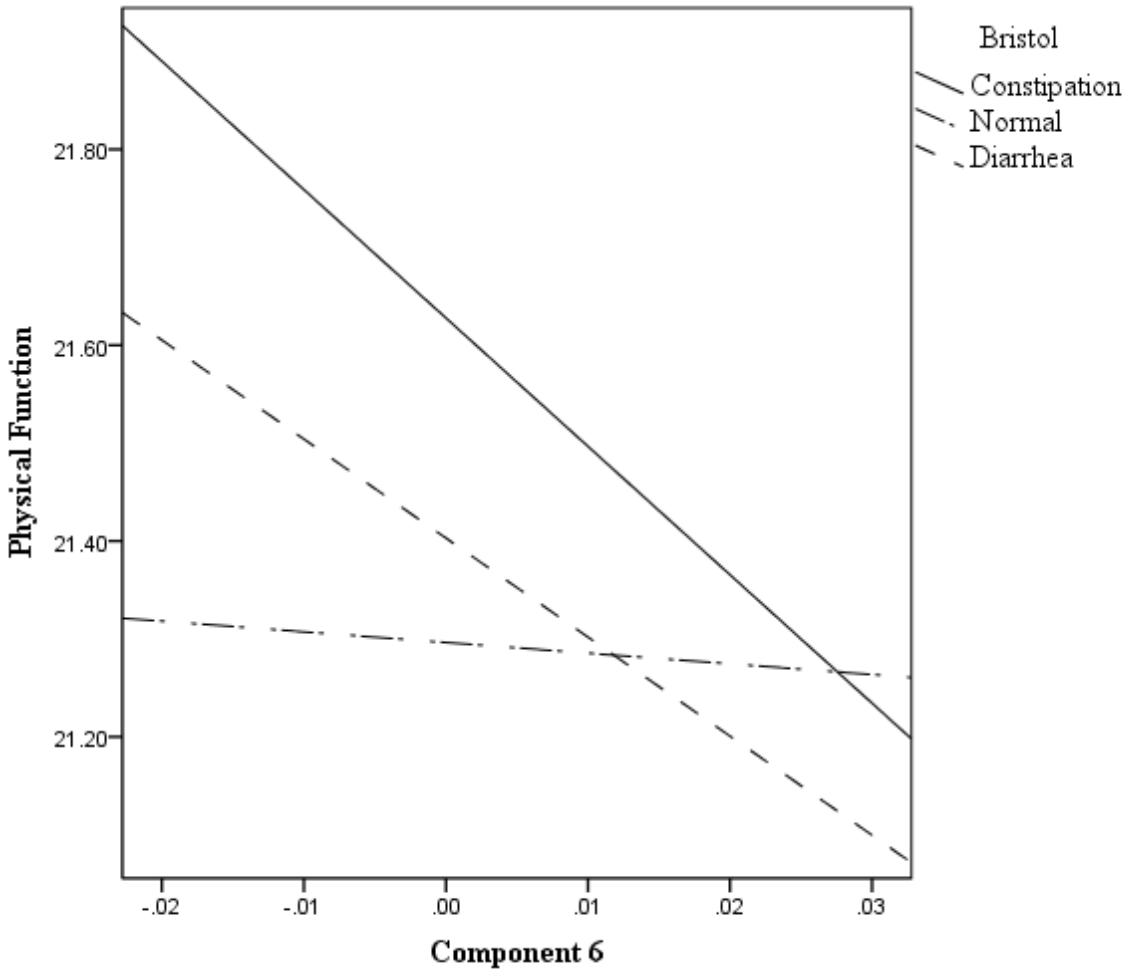

Figure 11: Moderating Effect of Bristol Stool among Component 6 and Physical Function

Note: Component 6 = MFA22_1, PFA18_4, PFA20_5, PFA22_5, and PFA22_6; Only the constipation and diarrhea group had a significant conditional effect

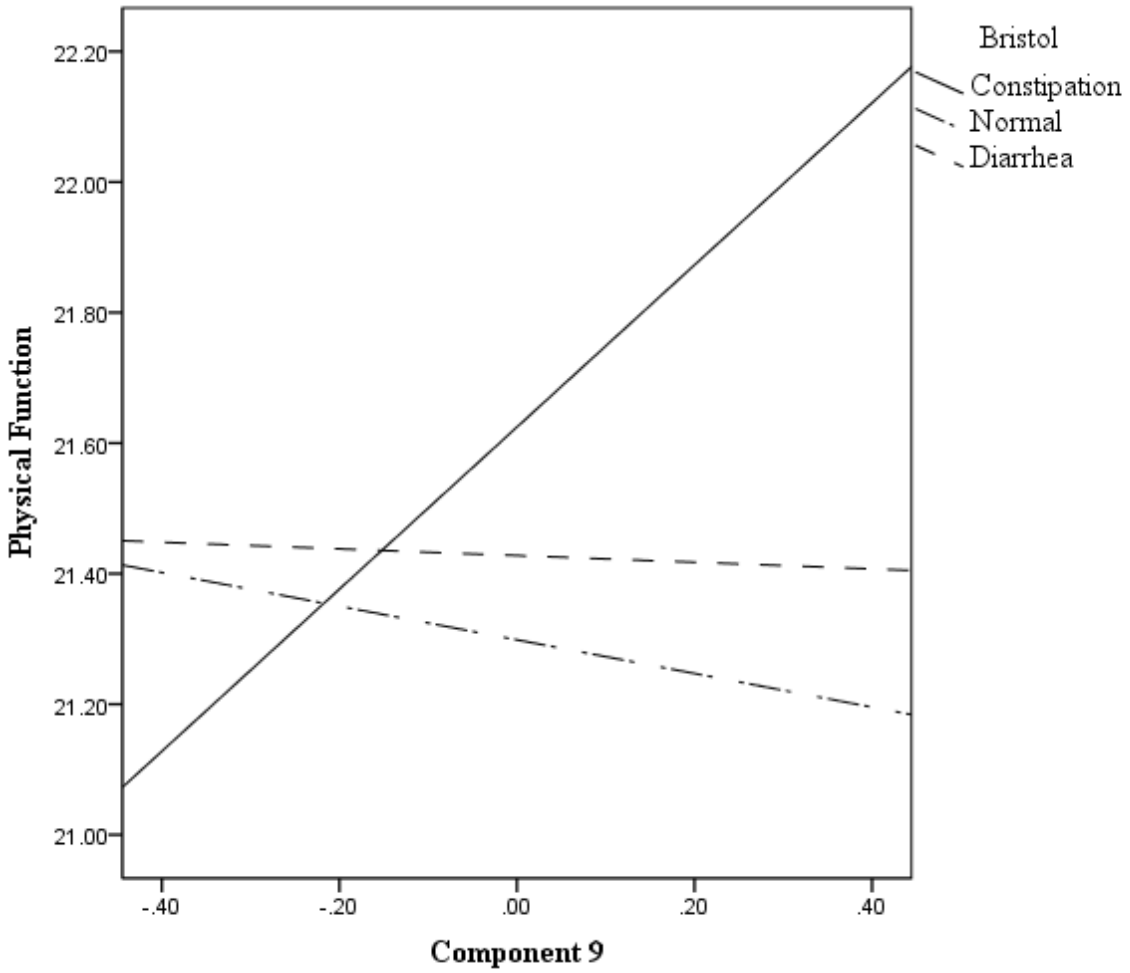

Figure 12: Moderating Effect of Bristol Stool among Component 9 and Physical Function

Note: Component 9 = Vitamin A and retinol; The overall model and the constipation group was near significant

Table 28: Demographic Characteristics for the Nutraceutical Blueberry Study

Characteristic	*N* = 108 *M* (%)	*SD*	Range
Demographics			
Age (y)	73.42	5.44	65-89
Ethnicity (white)	(96.20)		
Gender (female)	(66.00)		
Education	15.56	2.65	
Bowel Function			
Gastric Function	2.30	2.59	0-10
Low/High	(78.30)		
Gastrointestinal Inflammation	2.64	4.27	0-21
Low/High	(80.20)		
Small Intestines and Pancreas	6.15	7.77	0-51
Low/High	(68.90)		
Colon	4.22	6.14	0-35
Low/High	(81.10)		
Cognitive Measures			
Digit Symbol Substitution	50.87	10.61	31-84
Identical Pictures	44.16	9.59	27-71
Number Comparison	43.50	9.10	24-68
AVLT Immediate	8.60	2.98	0-14
Trail Making Test A	38.95	10.43	21-75
Trail Making Test B	1.91	0.16	1.58-2.48
AVLT Delayed	8.49	3.07	2-15
Digitspan Forward	10.44	2.11	6-15
Digitspan Backward	7.10	2.43	2-16
Category Fluency	15.95	4.96	2-27
COWA	40.30	11.58	19-86
Vocabulary	38.86	7.06	14-52

Table 29: Regression with AVLT and Bowel Function

Predictor	B Coefficient	*SE* B	R^2	ΔR^2
Model 1	-	-	0.140**	-
Constant	15.841***	3.752	-	-
Race	-2.875*	1.439	-	-
Gender	-1.133†	0.604	-	-
Age	-0.103*	0.050	-	-
Education	1.354*	0.580	-	-
Model 2	-	-	0.164	0.024
Gastric Function	0.104	0.122	-	-
Gastrointestinal Inflammation	-0.048	0.086	-	-
Small Intestines & Pancreas	0.051	0.062	-	-
Colon	-0.090	0.072	-	-
Quadratic Model 3	-	-	0.264*	0.101*
Gastric Function	-0.010	0.040	-	-
Gastrointestinal Inflammation	-0.033†	0.017	-	-
Small Intestines & Pancreas	-0.002	0.003	-	-
Colon	0.010†	0.005	-	-

****p<.001, **p<.001, *p<.05, †p<.10*

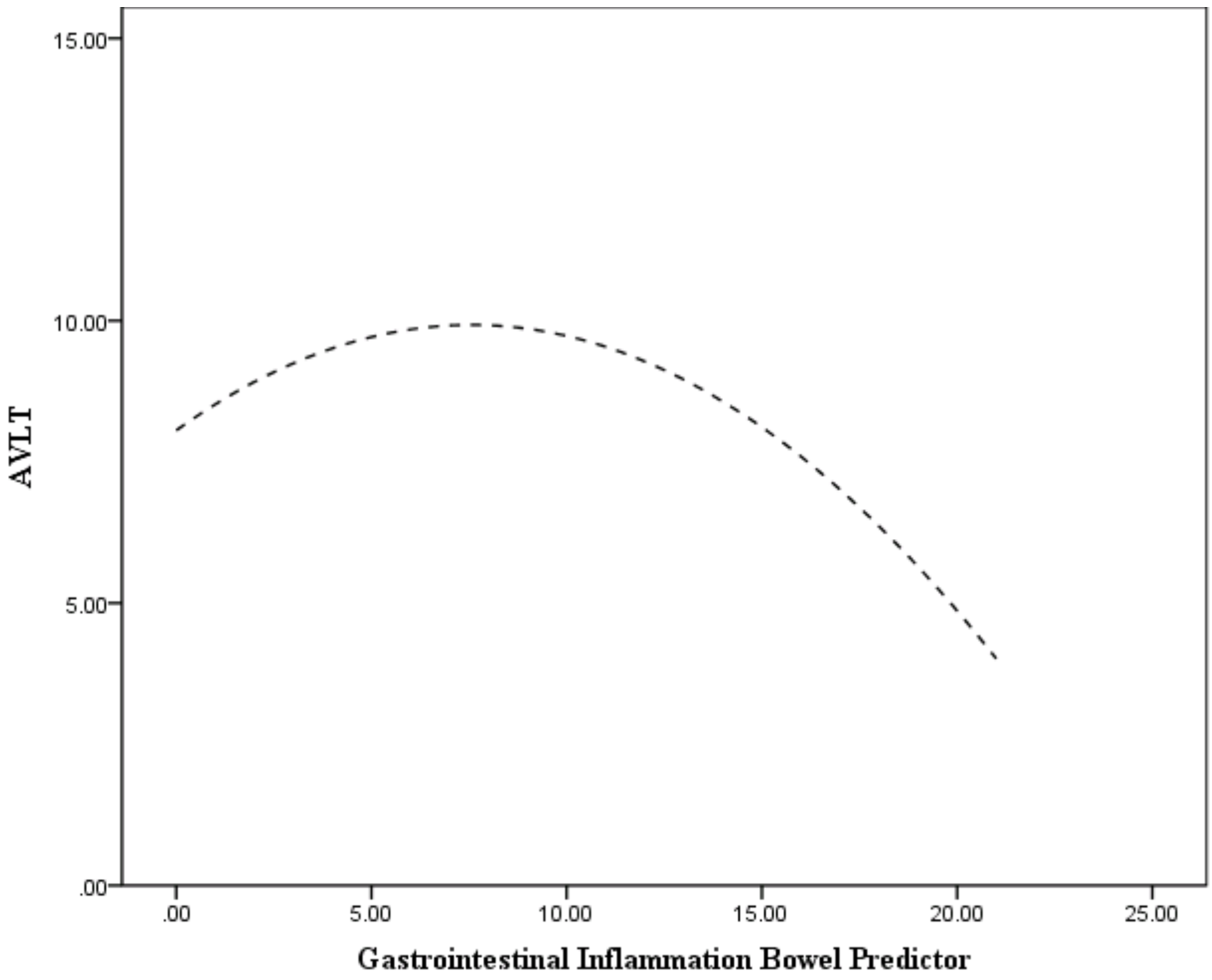

Figure 13: Curvilinear Regression Line for the Gastrointestinal Inflammation Bowel Predictor and AVLT

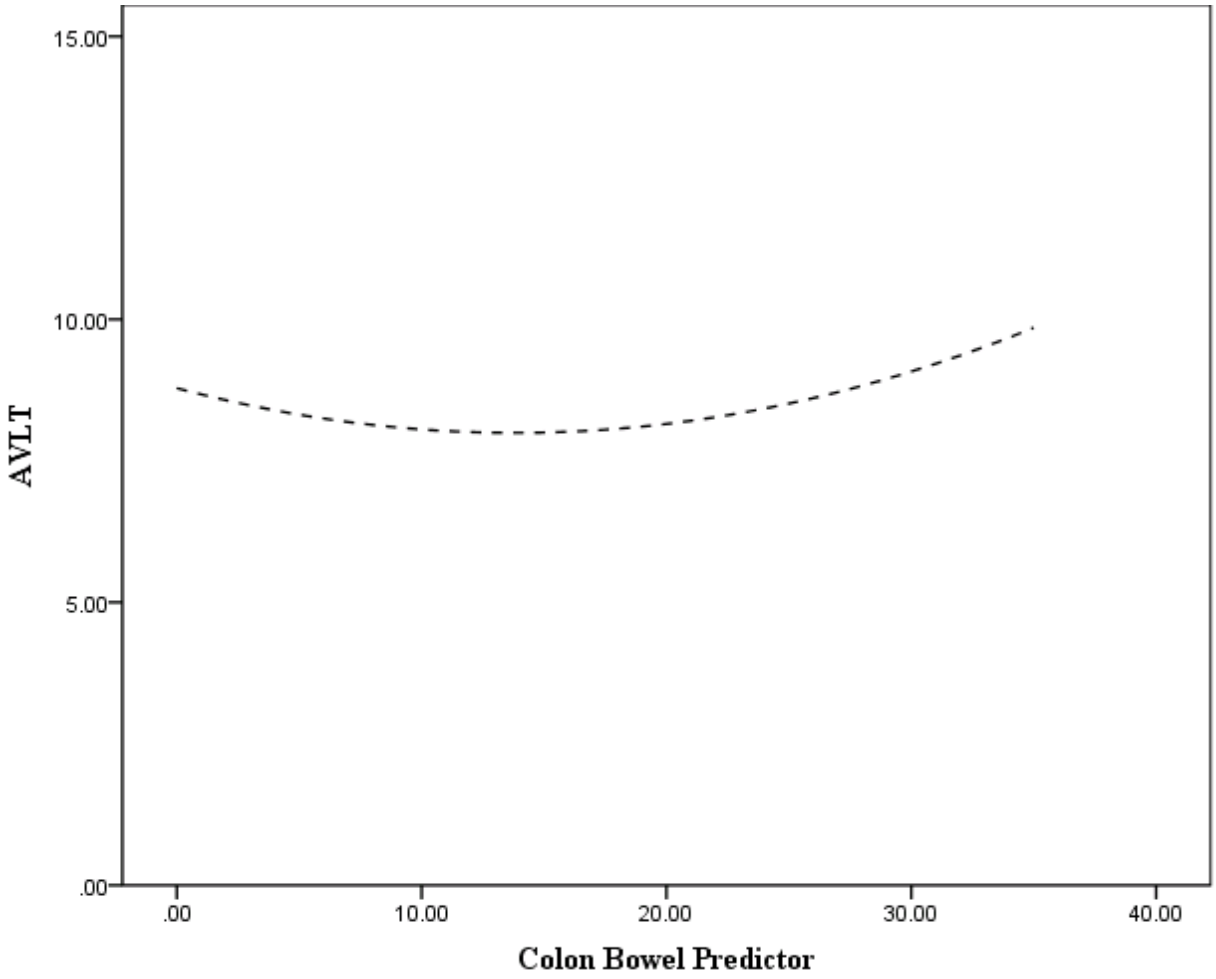

Figure 14: Fitted Curvilinear Line for the Colon Bowel Predictor for AVLT

Table 30: Regression with AVLT Delay and Bowel Function

Predictor	B Coefficient	*SE* B	R^2	ΔR^2
Model 1	-	-	0.204***	-
Constant	16.465***	3.784	-	-
Race	-3.886**	1.436	-	-
Gender	-1.883**	0.607	-	-
Age	-0.109*	0.051	-	-
Education	1.442*	0.579	-	-
Model 2	-	-	0.231	0.027
Gastric Function	0.116	0.121	-	-
Gastrointestinal Inflammation	-0.031	0.086	-	-
Small Intestines & Pancreas	0.043	0.062	-	-
Colon	-0.101	0.071	-	-
Quadratic Model 3	-	-	0.317*	0.086*
Gastric Function	-0.036	0.040	-	-
Gastrointestinal Inflammation	-0.032†	0.017	-	-
Small Intestines & Pancreas	-0.002	0.003	-	-
Colon	0.007	0.005	-	-

****p<.001, **p<.001, *p<.05, †p<.10*

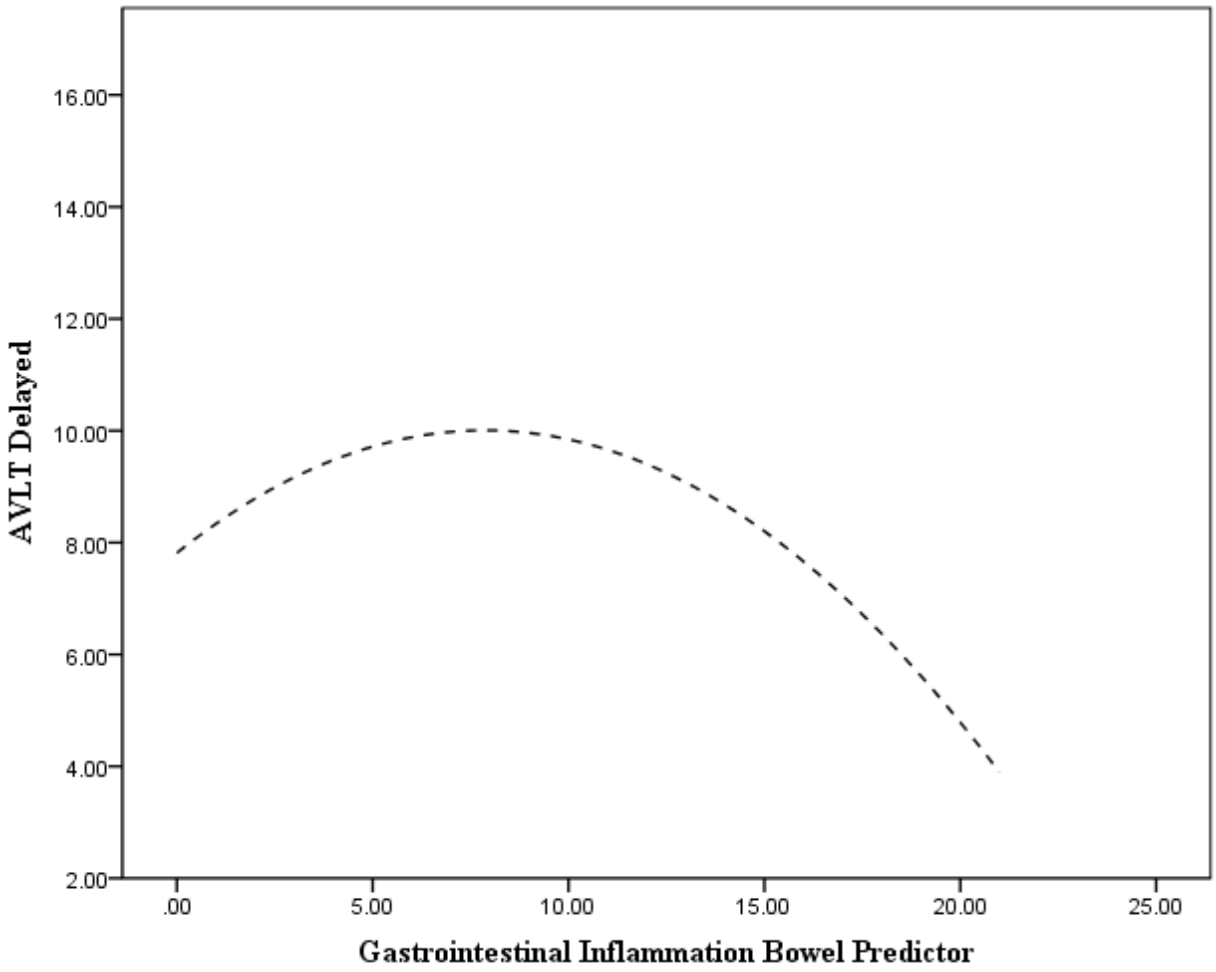

Figure 15: Curvilinear Regression Line for the Gastrointestinal Inflammation Bowel Predictor AVLT Delayed

Table 31: Regression with Category Fluency and Bowel Function

Predictor	B Coefficient	*SE* B	R^2	ΔR^2
Model 1	-	-	0.052	-
Constant	19.265***	6.571	-	-
Race	1.428	2.521	-	-
Gender	-2.204*	1.057	-	-
Age	-0.045	0.088	-	-
Education	1.105	1.016	-	-
Model 2	-	-	0.133†	0.081†
Gastric Function	-0.244	0.207	-	-
Gastrointestinal Inflammation	0.151	0.147	-	-
Small Intestines & Pancreas	0.017	0.105	-	-
Colon	-0.256*	0.122	-	-
Quadratic Model 3	-	-	0.210†	0.076†
Gastric Function	-0.020	0.069	-	-
Gastrointestinal Inflammation	0.040	0.030	-	-
Small Intestines & Pancreas	-0.011†	0.006	-	-
Colon	-0.008	0.009	-	-

****p<.001, **p<.001, *p<.05, †p<.10*

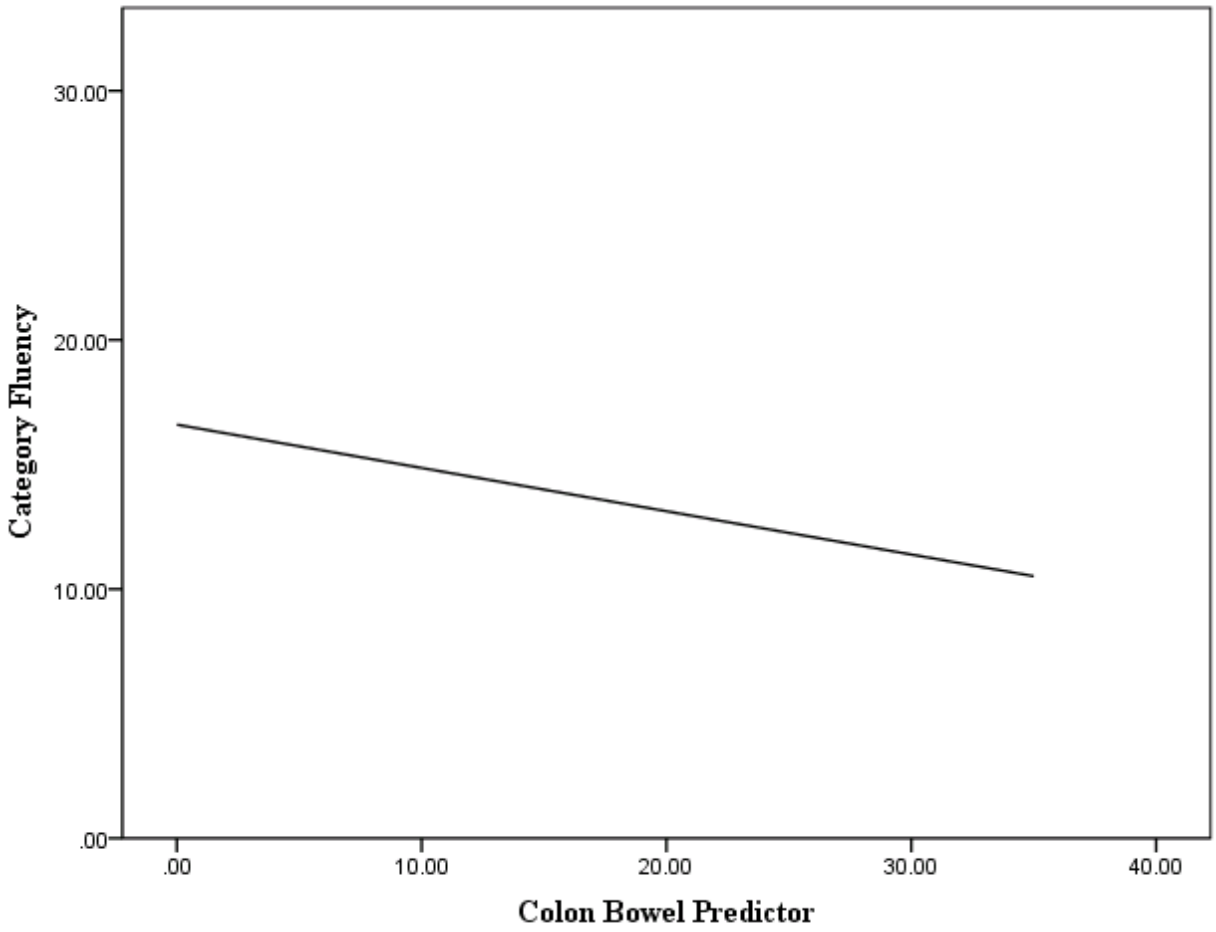

Figure 16: Fitted Regression Line for the Colon Bowel Predictor for Category Fluency

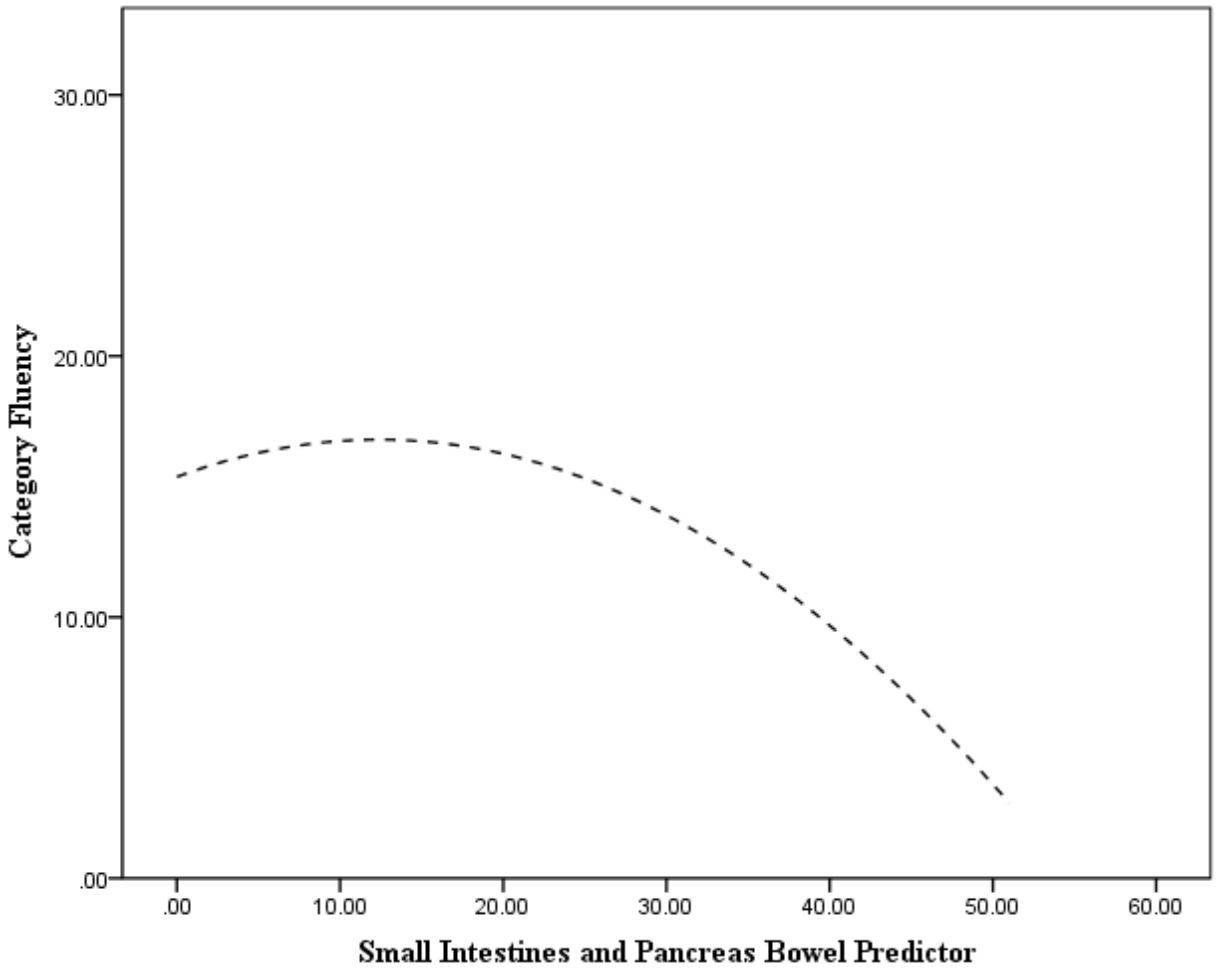

Figure 17: Curvilinear Regression Line for the Small Intestines and Pancreas Bowel Predictor and Category Fluency

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